PREVALENCE OF *HELICOBACTER PYLORI* IN DIABETIC AND NON-DIABETIC DYSPEPTIC PATIENTS IN BUNDELKHAND REGION

THESIS
FOR
DOCTOR OF MEDICINE
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BUNDELKHAND UNIVERSITY
JHANSI (UP)

2003 **VIKAS JAIN**

Dedicated

To

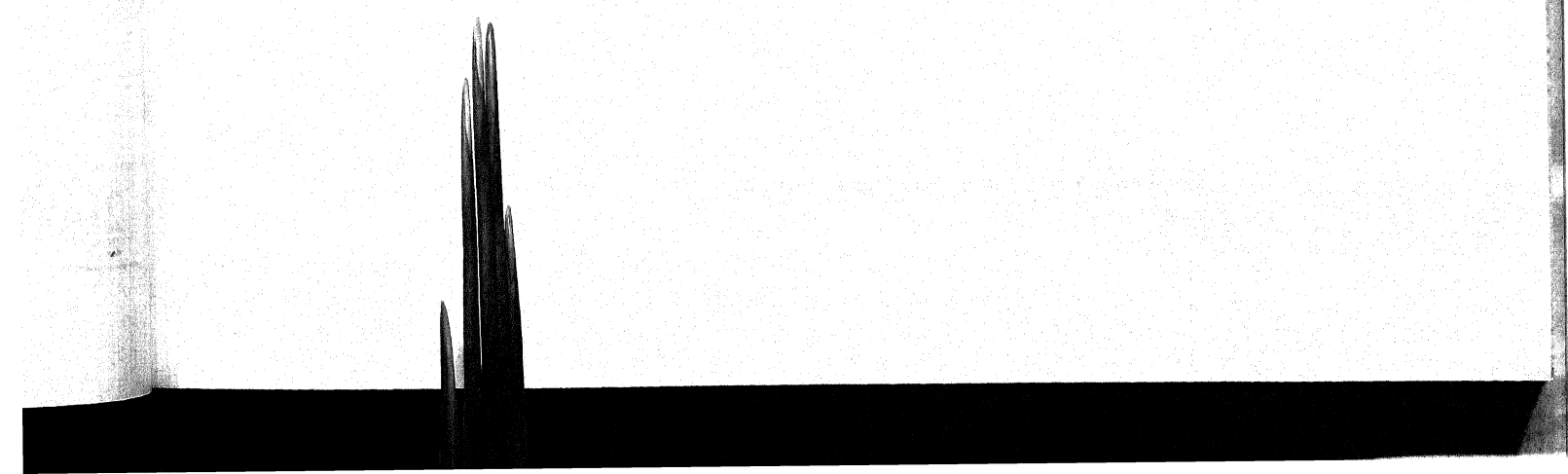
Respected

Teachers, Parents,

Friends

&

My Wife



CERTIFICATE

This is to certify that the work entitled "PREVALENCE OF *Helicobacter pylori* IN DIABETIC AND NON-DIABETIC DYSPEPTIC PATIENTS IN BUNDELKHAND REGION" which is being submitted as a thesis for M.D. (Medicine) Examination 2003, of Bundelkhand University, has been carried out by **Dr. Vikas Jain** under my direct supervision. The techniques embodied in this thesis were undertaken by the candidate himself and the observations recorded were checked and verified by me from time to time.

7/07/03
Dated:

Prof. R.C.Arora MD, DSc
Head of the Department,
Department of Medicine,
MLB Medical College,
Jhansi

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Dated:

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Dated :

Vikas Jain

CONTENTS

INTRODUCTION

INTRODUCTION

Dyspepsia, which has been defined as recurrent upper abdominal or retrosternal pain, vomiting or other symptoms felt to be referable to the upper GI tract [1], is by far the commonest ailment, demanding maximum consultation in any outpatients department of Gastroenterology.

A multitude of causes have been implicated in the symptoms of dyspepsia of which gastritis, peptic ulcer, esophagitis and cancer are only to name some.

The first reports of the association of dyspepsia with *Helicobacter pylori* came in the late seventh and early eighth decades when *Steer HW (1975)* reported a spiral bacterium in 80% of specimens resected from patients with gastric ulceration [2]. These bacteria were micoraerobic, curved, Gram negative and resembled Campylobacters; they were therefore called *Campylobacter pyloris*. The genus *Helicobacter* was suggested in 1989 when the organisms showed differences with *Campylobacter*.

Upper gastrointestinal tract abnormalities ranging from gastroparesis to minor dyspeptic symptoms are frequent in patients suffering from long standing Diabetes mellitus [3]. The pathogenesis of these symptoms is poorly understood. But it is thought that

gastrointestinal motility disturbances related to autonomic and vagal neuropathy may be involved.

Labenz J et al and *Fisher RS et al* in different studies speculated that *Helicobacter pylori* infection could play a role [4, 5].

Data concerning the prevalence of *Helicobacter pylori* infection in patients with diabetes are scanty and controversial; various studies have however been conducted to establish this association.

Gasbarrini A et al (1998) noted that patients affected by insulin dependent diabetes mellitus show a high prevalence of *Helicobacter pylori* infection.

The reason for this association may be multifold. One of these may be the increased susceptibility of diabetics to be infected by bacteria and fungi far more than healthy subjects [6].

This susceptibility may also be due in part to neutrophil dysfunction with failure of chemotaxis, phagocytosis and in part to the reduction of lymphocytic activity so commonly associated with diabetes [7].

Diabetes is characterized by autonomic neuropathy and microvascular disorders. In particular 40-50% of diabetes patients have gastric motility disturbances such as delayed gastric emptying.

Chia Hung Kao et al (1995) attempted to establish a relationship between *Helicobacter pylori* infection and delayed gastric emptying times.

Together with neuropathy, another important feature of diabetes is the development of microvascular complications that could be the result of long-standing functional abnormalities in the microcirculation such as altered capillary pressure, blood flow and permeability, which are present from an early stage in the course of diabetes. These factors may again predispose to an increased prevalence of *Helicobacter pylori* infection.

The current approach in diabetes management is to give the patient a symptom free life with adequate blood sugar control and prompt and active management of complications.

In accordance with this approach it is desirable to finely scrutinize these symptoms and their etiology. Awareness of the correct etiology is central to the management of any ailment. Establishment of an association of *Helicobacter pylori* with dyspepsia in diabetes will therefore revolutionize its treatment; as the treatment of *Helicobacter pylori* infection is increasingly becoming simple and effective. "Standard triple therapy" given for two weeks eradicates *Helicobacter pylori* in 90% of cases [8].

The present study aims at accumulating evidence for an association of *Helicobacter pylori* with dyspepsia in diabetes by comparing the prevalence of *Helicobacter pylori* in diabetic dyspeptic and non-diabetic dyspeptic patients.

REVIEW OF LITERATURE

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Robin Warren and Barry Marshall who first identified *Helicobacter pylori* (1983) described it as unidentified curved bacillus in close contact with gastric epithelium in biopsy sample showing active chronic gastritis. [9] In human stomach it has been found on luminal aspect of surface mucous secreting cell, underneath the surface of mucous within gastric pits *(Tricaltet C, Bruneva P, Camilleri H. 1986).[10]* This location protects it from gastric acid to which it is sensitive *(Rollason et al. 1984)[11]. Mc. Nulty et al 1985) [12]* found that *Helicobacter pylori* shows significant urease activity – a property that has been adopted for rapid diagnostic test for organism. This enzyme also helps in creating basic environment around bacteria thereby protecting it form acid media of stomach.

Helicobacter pylori is rarely seen in histologically normal antral mucosa, but if present almost always shows histological evidence of chronic type B. gastritis *(Marshall and Warren 1984, Mcnulty and Wattson 1984, Rollson et al. 1984).*[9,12,13]

THE ORGANISM – HELICOBACTOR PYLORI:

When originally isolated, *Helicobacter pylori* was thought to be a member of genus campylobacter, but subsequently work has shown to

be the first member of new genus Helicobacter *(Goodwin CS, Armstrong JA et al. 1986).* [14]

Helicobacter pylori is worldwide in distribution, gram negative, micro aerophilic, spiral, nonsporing, motile bacilli, measuring, 0.5 μm x 3μm in size. When seen under electromicroscopy it has smooth wall and 4-6 sheathed flagellae projecting from either pole each with terminal bulb *(Goodwin et al. 1985)[15].* It differs from campylobacter species which have unsheathed non bulbous flagellae and rugose cell wall. They have less urease content and they can reduce nitrate. *Helicobacter pylori* is an acid sensitive bacteria and lies in mucous layer which overlies epithelial cells in alkaline environment. One of the characteristic of *Helicobacter pylori* is possession of powerful urease, which may be responsible for its ability to survive in acidic environment of gastric lumen. The ammonia produced raises pH in its immediate vicinity and may protect it (*Marshall BJ, Barrett L, Prakash et al. 1988).[16]*

EPIDEMIOLOGY OF HELICOBACTER PYLORI:

Our undersanding of the epidemiology of Helicobacter pylori infection in the general population is rapidly increasing. The infection seems to be acquired early in childhood and persists throughout life *(Cullen DJE et al 1993)[17].* Most infected individuals do not develop

symptoms. Although type B chronic gastritis appears in the antral biopsies of all infected subjects (*Drumm B et al 1987)[18]*.

The prevalence of the infection in adults is 30-35% in developed and 80-90% in developing countries (*Taylor DN et al 1991)[19]. Helicobacter pylori* infection in the general population correlates strongly with age (*Teh BH et al* 1994; *Taylor DN et al 1991)[19,20],* social class , educational level (*The EUROGAST Study Group, 1993)[21]* and overcrowding, bed sharing, and economic level during childhood (*Patel P et al 1994)[22].* The rise of prevalence in older patients is due to a cohort effect, reflecting an increased risk of exposure during childhood rather than a continued risk of infection during adult life (*Teh Bh et al 1994).[20]*

TRANSMISSION:

High prevalence of *Helicobacter pylori* seen in some social groups such as homosexuals, and institutionalized mentally retarded patient, demonstrates man to man transmission. (*Aceti et al.* 1987).[23]

The *Helicobacter pylori* occurs in two morphologic forms (*Bode G. et al.* 1988)[24]. The typical replicative form is gram negative curved rod with 4-6 flagella, which converts to a coccoid form if allowed to grow for more than a few days on a culture plate. The coccoid form is of variable size, may or may not be flagellated.

The replicative form of *Helicobacter pylori* has been demonstrated to survive in water upto a week. While the coccoid form is a potential "Spore" candidate, there is no evidence to suggest that this is transmissible form of *Helicobacter pylori.*

The meat handlers are more prone to *Helicobacter pylori* infection than other people (*D. Annastasio et al.* 1988).[25]

Infection has strong intrafamlial clustering, suggesting a person to person transmission in industrialized countries (*Malaty HM. et al.* 1991).[26] By contrast, the infection is probably waterborne in developing countries (*Klein PD et al.* 1991).[27]

STRAIN HETEROGEITY AND VIRULENCE:

Most strains of *Helicobacter pylori* causes gastritis while infection with some strain may lead to more serious manifestation. To date four phenotypes that vary among *Helicobacter pylori* strains have been identified. Approximately 60% of *Helicobacter pylori* strain possess cag-A gene which encodes Cag-A protein. At present Cag-A genotype is thought to be associated with peptic ulcer disease while other strains are associated with simple gastritis (*Cover et al.* 1990) [28]. Recent work has identified a region of DNA in chromosome of *Helicobacter pylori* that is unique to some strains. This "pathogenicity island" which appears to include cag-A gene, have been preliminarily characterized

by nucleotide sequencing and are responsible for virulence of some strains.

COLONIZATION:

The first step of infection requires that *Helicobacter pylori* must colonize the gastric mucosa. This process may take upto a week to complete. The organism must enter the stomach, survive brief exposure to acid, enter and successfully traverse the mucous layer, attach to epithelial cell receptor and adopt its physiology to the hostile environment. Urease is most prominent protein component of *Helicobacter pylori* and is critical for colonization of gastric mucosa. Urease produces alkaline media around bacillus, by producing ammonia from urea and protect it from hostile environment. Urease negative strain of *Helicobacter pylori* were unable to colonize the gastric mucosa, indirectly suggesting that urease is necessary for colonization (*Eaton KA et al.* 1992).[29]

The extraordinary motility of *Helicobacter pylori* through mucus is mediated by the polar flagella and it is thought that this process may help colonization (*Eaton KA Morgan DR* 1992).[29] Indeed flagella negative mutant of *Helicobacter pylori* are unable to colonize the gastric mucosa of antibiotic piglets. Although there is no direct evidence that adhesin are required by *Helicobacter pylori* to colonize but since *Helicobacter pylori* exhibits remarkable tissue and host specificity (i.e. it

binds to normal and metaplastic gastric epithelium), the existence of tissue specific adhesins seems to be extremely likely. There is also good evidence to suggest that *Helicobacter pylori* produces an acid inhibitory protein that blocks acid secretion from parietal cells. (*Cave et al.* 1989, *Jablonowski H. et al.* 1994).[30,31]

TESTING FOR HELICOBACTER PYLORI IN CLINICAL PRACTICE:

Two major categories of diagnostic tests for H. Pylori are available;- invasive and non-invasive methods.

(A) INVASIVE DIAGNOSTIC TESTS:

(1) Rapid Urease Test-

Rapid urease test has high specificity and moderate sensitivity (*Veldhugzen Van Senten SJO et al.* 1991)[32]. It is based on the principle that *Helicobacter pylori* has very high urease activity making it's detection possible by observing a change in colour of indicator due to hydrolysis of urea to ammonia, in a media containing agar, urea, phenol red (indicator), at pH 6.8 and a bacteriostatic agent. The change of colour of medium from yellow to dark pink indicates a definite presence of *Helicobacter pylori* in biopsy specimen. The colour change is very rapid and takes place within 20 minutes to four hours or rarely it may take 8 -24 hours. Various kits are also available. Modified christensons urea media on agar slant in 'Kahn' test tube (*Nanivadekar*

1989),[33] liquid urea broth, phenol red or bromothymol as indicator (*Hazell SL et al.* 1986) [34] can also be used for detection of *Helicobacter pylori.* The rapid urease test is based on the presence of adequate number of bacteria with urease activity. Test sensitivity, therefore can be affected by use of agent that reduces gastric bacterial load or directly inhibits enzyme activity.

(2) Histology:

Two or more antral biopsies with hematoxylin and eosin staining should be sufficient to establish infection status in an untreated patient. *Helicobacter pylori* is distributed throughout the gastric mucosa, although its presence can be patchy. The presence of chronic active gastritis in an untreated patient should strongly suggest active infection. The absence of chronic mucosal inflammation reliably excludes *Helicobacter pylori* infection (*Culter AF Havstad et al.* 1995).[35]

The warthin silver stain (*Warren R. Marshall B.* 1983)[9] enables accurate identification

(3) Culture:

The use of microbiological culture of gastric biopsies is limited due to the expense, limited availability and fastidious nature of the organism. (*Barthel JS et al.* 1990).[36] However the expected emergence of multiple antibacterial resistance among *Helicobacter pylori* may necessitate the increasing use of culture by clinical

gastroentrologist. There are many satisfactory culture media for *Helicobacter pylori*, most are blood enriched and contains appropriate antibiotic and/or antifungal agent (*Skirrow Formula*) to avoid overgrowth by oral bacteria (*Good Win et al. 1985*)[15]. *Helicobacter pylori* is fastidious bacteria and requires microaerophilic environment, with, 10% Co_2 at 37°C. It grows in 3-7 days, identification of *Helicobacter pylori* was based on colony morphology and visualization of gram-negative rod, which is urease positive. Culture sensitivity is 85-90% in most developed centre of world *(Marshall BJ et al ,Goodwin et al. 1985)*[9,15] and 30-60% in India (*Nanivadekar et al.* 1989)[33].

(4) Other invasive tests:

Two other invasive test are available includes polymerase chain reaction (PCR) and phase contrast microscopy. PCR is research tool while phase contrast microscopy requires dark field examination of fresh gastric biopsies.

(B) NON- INVASIVE DIAGNOSITIC TESTS :

(1) Antibody Detection –

Chronic *Helicobacter pylori* infection elicits local and systemic immunologic responses leading to production of 1gG and 1gA antibodies. In general the measurement of serum 1gG level is preferred test basis, as level of this antibody is more accurate for infection status (*Perez-Perez* 1989)[37]. The diagnostic tests that detects *Helicobacter pylori* antibodies are inexpensive global test with typically high specificity and sensitivity (*Talley NJ et al,* 1992) [38]. Separated serum is subjected to quantitative ELISA test or qualitative in office immunoassays. Antibody detection has limited use in post treatment period. Immunoassays and whole blood are qualitative tests that will remain positive in post treatment period and therefore can not be used to determine bacterial eradication.

(2) Urea Breath Tests – (UBT) -

UBT will probably be optimum choice to confirm eradication in patient with complicated ulcer and in those patient with recurrent symptoms following treatment of *Helicobacter pylori* Although the test can be used to confirm eradication, test must be performed at least 4 week after completion of treatment. *(Logan RPH et al. 1995)*[39]. The UBT may have lower sensitivity in patient who have had previous gastric resections, as the contact time between bacteria and substrate will be reduced *(Well J. Bell GD et al. 1991)*[40].

CHOOSING A TEST:

Sensitivity, specificity and negative and positive predictive value ofsevendiagnostic test for *Helicobacter pylori* are given below:-

PARAMETERS	Sensitivity (%)	Specificity (%)	PREDICTIVE VALUE	
			Positive (%)	Negative (%)
INVASIVE –				
-Chronic inflammation in Biopsy	100	66	84	100
-Acute Inflammation in Biopsy	87	93	96	79
-Rapid urease test	90	100	100	84
NON-INVASIVE -				
- UBT	90	96	98	84
- S. IgG	91	91	95	85
- S. IgA	71	85	90	62

Accuracy of modality, cost of the test, whether upper GI endoscopy is planned and clinical circumstances all are considered while choosing a test.

Any of the biopsy based methods that are rapid urease test culture and histology are not sufficient alone for the diagnosis of *Helicobacter pylori.* However, they should be recommended when endoscopy is performed, since isolation by culture and histology will provide additional information about antibiotic susceptibility, the type and severity of inflammatory changes in the mucosa and also of pre-malignant changes if any.

The definition of a 'gold standard' seems to be difficult. Previously, either culture of *Helicobacter pylori* or demonstration of HLO in histologic sections was regarded as the 'gold standard'. Later it has been proposed that a third test (UBT, CLO test, or serology) should be included, and the *Helicobacter pylori* status is considered positive when one or more of three tests is positive.

In conclusion, it is recommended that a reliable evaluation by diagnostic tests include at least one test from each group of methods based on different principle and that the 'gold standard' should be regarded as two positive of these five tests.

DYSPEPSIA

Dyspepsia is a common complaint, with a prevalence of 14% to 26% if predominant reflux symptoms are excluded[41]. The prevalence of dyspepsia is higher among women and, somewhat surprisingly, is stable or even declines with age[42,43].

Dyspepsia has been defined as 'reccurent upper or retrosternal pain, vomiting or other symptoms felt to be referable to upper GI tract'.[1] *Talley et al* proposed that it should be defined as pain or discomfort centered in the upper abdomen present for at least a month[44].

The prevalence of dyspepsia in the community over a 6 month period is about 40%, with 70% of the population having experienced this symptom at sometime in the past[45]. The majority of dyspepsia sufferers have mild symptoms not interfering with their lives or relieved by over-the-counter medications.

In a study of dyspepsia in the community by *Lydeard S, Jones R.1998,* 48% were sufferers, and of these 70% reported mild symptoms and 9% reported severe symptoms,but was determined by fear of serious pathology and low socio-economic group[46].

According to *Jones RH.1993*,dyspepsia comprises about 5% of general practice consultations, with only 10% of these being referred for further specialised evaluation in hospital[47].

Knill-Jones RP.1991, in his study found that consultation for dyspepsia account for up to 40% of referrals to gastro-enterology outpatients[48].

Nicholas J, Talley et al (1993),[49] based on their responses to the questionnaire, classified the patients with dyspepsia into the following symptoms subgroups-[49]

1. **Ulcer like dyspepsia**.

This was defined as dyspepsia and three or more of the following symptoms: abdominal pain or discomfort before meals or when hungry often or usually; night pain (waking the subject from sleep); pain or discomfort relieved by food often or usually; pain or discomfort relieved by antacids often or usually; periodic pain or discomfort; and well-localized abdominal pain or discomfort.

2. **Dysmotility like dyspepsia**.

This was defined as three or more of the following symptoms: nausea once a month or more; retching or vomiting once a month or more; upper abdominal bloating usually, In the absence of visible distension; early satiety often or usually; upper abdominal pain or

discomfort aggravated by food or milk often or usually; and postprandial upper abdominal pain or discomfort often or usually.

3. **Reflux like dyspepsia**.

This included dyspepsia and heart-burn or acid regurgitation once a week or more.

4. **Nonspecific dyspepsia**.

This included dyspepsia with symptoms not fitting into categories1,2,or3.

Armstrong D.1996 and Talley NJ.1996[50,51],on the basis of endosopy report classified the patients in to following diagnostic groups-

1. **Functional or Non-ulcer dyspepsia.**

This was defined as documented upper abdominal pain or discomfort, with essentially normal endoscopical findings (no esophagitis, erosions, chronic peptic ulceration, or gastric cancer).

2. **Chronic peptic ulceration**.

This was defined as a >3mm ulcer with depth in the stomach and/or duodenum at endoscopy. Gastric ulcers were included in this group only if malignancy was ruled out.

3. **Acute peptic ulceration.**

This was defined as a <3mm erosion without depth in the absence of chronic peptic ulceration.

4. **Reflux esophagitis.**

Defined as endoscopic evidence of gastroesophageal reflux (GER),using the *Savary-Miller grading system*[52] as follows -

Grade 1- Linear, nonconfluent erythema or erosions

Grade 2- Longitudinal, confluent, noncircumferential erosions.

Grade 3- Longitudinal, confluent, circumferential erosions that may bleed easily.

Grade 4- Esophageal ulceration and/or presence of a peptic stricture.

5. **Gastric carcinoma.**

Confirmed by biopsy

HELICOBACTER PYLORI AND DYSPEPSIA

Helicobacter pylori is a major etiological factor in peptic ulcer disease. About 95% of patients with duodenal ulcers and perhaps 80% of gastric ulcers are infected with this bacterium and it's eradication greatly diminishes recurrence of these ulcers.

A peptic ulcer is a breach in the gastric or duodenal epithelium associated with acute and chronic inflammation. In most countries, duodenal ulcers are about 3 times more common than gastric ulcers.

Ihamaki T, Varis K et al(1979)[53], in their study conducted in Finland, found that at any time 1.4% of a population had duodenal ulcer, whereas 0.3% of the population had chronic gastric ulcer.

Langman MJS(1979) found lifetime prevalence of duodenal ulcers to be 10% in males and 4% in females and of gastric ulcers to be 4% in males and 3% in females[54]. The incidence of duodenal ulcers gradually rises with age but peaks at about 60 years of age. The prevalence of gastric ulcers was found similar in males and females .They were rare under the age of 40 years and tend to occur in the lower socio-economic groups[54].

Marshall BJ,Warren JR (1984)[9] found that the stomach, which was previously thought to be sterile, is frequently infected with *Helicobacter pylori* and, moreover, that > 90%of duodenal ulcer patients are infected compared with about 40% of controls.

Marshall BJ, Goodwin CS et al 1988,[55] observed that eradication of *Helicobacter pylori* greatly diminishes the recurrence rate of duodenal ulcer.

In the studies done by *Rauws EA,Tytgat GN,1990* in Amsterdam the recurrence rate was zero so that disease was regarded as cure[56].

Hopkins et al[57]reviewed 14 duodenal ulcer eradication studies and noted overall recurrence rate of 6% following successful eradication of *Helicobacter pylori* compared with 67% when infection remained.

According to *McColl KE et al,1993*, rate of recurrence after successful eradication may also depend on how carefully the less common causes of duodenal ulceration; NSAIDs, Crohn's disease, gastrinoma, are excluded[58].

*Huang JQ et al 1996,*observed that apart from diminishing recurrence, eradication of *Helicobacter pylori* leads to faster healing of duodenal ulcers than suppression of acid secretion alone[59]

According to *Lanas AI et al1995,*a substantial minority of gastric ulcer patients are genuinely not infected and have ulcers due to ingestion of NSAIDs, which may be denied by as many as 44% of patients[60].

However, it is now clear that eradication of *Helicobacter pylori* from infected gastric ulcer patients who are not taking NSAIDs greatly diminishes the recurrence of these ulcers. *Graham et al* reported 2 year relapse rates of 13% after ranitidine plus triple therapy, compared with 74% in patients given ranitidine alone[61].

Karita et al reported 1 year gastric ulcer relapse rates of 0% after successful eradication compared with 75% in those with persisting infection[62].

Bayerdorffer reported recurrence rates of 2% and 49%, respectively, in gastric ulcer patients who had or had not *Helicobacter pylori* eradicated during endoscopic follow up for 18 months[63].

In a Meta-analysis of 5 trials, *Hopkins et al* noted a gastric ulcer recurrence rate of 4% after successful eradication, compared with 59% when the infection persisted [57].

Labenz et al found that gastric ulcers heal more rapidly if the regimen eradicates the infection. The rate of ulcer healing at 6 weeks was 85% if the bacterium was eventually eradicated compared with 60% if it was not [64].

Hawkey CJ [1990] in his study relating NSAIDS and peptic ulcers found that of patients taking NSAIDs, 8-16% have gastrointestinal symptoms at any time, and the potential of NSAID-ulcers to bleed or

perforate is considerable, particularly in the elderly who cope with these complications badly[65].

Griffith MR et al (1991) documented that NSAIDs causes gastric ulcers more often than DUs. Early damage consists of multiple erosions. gastric ulcer Chronic ulcers which are larger and deeper, appear later[66].

Lipscombe et al(1996) examined the effect of *Helicobacter pylori* status on acute NSAID - induced gastric damage. They gave naproxen 500 mg b.d. to 24 healthy volunteers for 4 weeks and found that the *Helicobacter pylori* status had no effect on mucosal blood flow or gastric mucosal damage[67].

Bianchi- Porro et al (1996)[68] studied arthritis patients taking long- term NSAIDs and had chronic ulcers with *Helicobacter pylori* infection.They were randomised to receive either omeprazole for 4 weeks with amoxycillin or omeprazole alone,whilst uninfected patients with arthritis also received omeprazole. Ulcer healing did not differ between the 3 groups. However, there was a trend to more frequent recurrence in those with persisting infection (46%) compared with those uninfected (27%).

In short, therefore, currently available data, including randomized trials, give inconclusive results, but leave open the possibility that

Helicobacter pylori exacerbates the tendency of NSAIDs to cause chronic ulcers.

Several studies have compared the prevalence of *Helicobacter pylori* in symptomatic and asymptomatic individuals. While some investigators have reported a higher prevalence of *Helicobacter pylori* in dyspepsia than in controls, others have found no difference in the prevalence between the two groups, or even a higher prevalence in the controls.

Bemersen et al(1992)[69] endoscoped 309 subjects with dyspepsia and 310 controls in an elegant Norwegian population- based study. They found that , overall , 48% of dyspeptic subjects had *Helicobacter pylori* compared with 36% of the controls , which was a significant difference; the prevalence was 53% and 35% , respectively in dyspeptic subjects and controls with normal endoscopic findings.

Schlemper et al (1995)[70] reported that anti- H. pylori IgG antibodies were present in 25% of individuals with non ulcer dyspepsia and 29% of those without non ulcer dyspepsia.

Early therapeutic clinical trials in *Helicobacter pylori* – positive patients with non ulcer dyspepsia provided very conflicting results. *Talley NJ(1994)* analysed 16 published trials; eight reported that anti-H.pylori therapy was efficacious and eight failed to detect a statistically significant benefit[71].

Laheij et al (1996), an a meta –analysis, reported that symptoms improved in 73% of the patients who became *Helicobacter pylori* – negative and in 45% of those with persistent infection.If eradication of *Helicobacter pylori* failed, symptoms only improved for a short period of time but, when *Helicobacter pylori* was eradicated, symptom improvement appeared to be more pronounced[72].

Elta et al[73] treated both *Helicobacter pylori* infected and uninfected patients with a double therapy but observed similar symptom improvement in both groups, with a mean follow-up of 34 months.

Murakami et al[74] have observed that gastric emptying significantly improved in 7 of 11 patients whose infection was eradicated and whose symptoms disappeared, but this needs to be confirmed.

Gastric cancer is the second most common fatal malignancy in the world and is the cause of more than 750000 deaths annually [75]. The evidence supportive of an etiological association between *Helicobacter pylori* infection and gastric cancer was sufficient for a Working Group of the International Agency for Research on Cancer to classify such infection as a definite cause of cancer[76].

Kuipers EJ et al (1995)[77] in a longitudinal study, comparing *Helicobacter pylori* positive to negative individuals over a 11 year period, established that there was a significantly increased risk of developing precancerous gastric conditions associated with infection

and reported an odds ratio of 9.0 (95% confidence intervals, 1.9 - 41.3),

Goodman KJ (1995) [78] added that much of the descriptive epidemiology of gastric cancer parallels that for *Helicobacter pylori* infection , most notably the strong association of both cancer and infection with poor socio-economic conditions.

Pisani P et al (1997)[79] estimated the risk and indicated that 53% and 60% of gastric cancers in the developing and developed world respectively, can be attributed to *Helicobacter pylori.*

There is much that remains to be established about the relationship between *Helicobacter pylori* infection and gastric cancer. Some epidemiological features of gastric cancer can not be explained by the infection, for example the male to female ratio of gastric cancer is usually in the order of 2.1 in nearly all populations [80], whereas *Helicobacter pylori* prevalence rates usually do not show any consistent sex difference [81].

Primary gastric lymphoma comprises about 3-6% of all gastric malignancies. Almost all are B cell non- Hodgkin's lymphomas most commonly of high grade. Gastric T cell lymphomas and Hodgkin's disease are extremely rare. In 1983, *Isaacson and Wright*[82] recognised that the low grade B cell lymphomas that arose specifically

within dedicated extra nodal lymphoid tissue known as mucosa associated lymphoid (MALT).

The most frequent event asoociated with the finding of organised lymphoid tissue in the gastric mucosa is infection with *Helicobacter pylori* [83]. In the most comprehensive study by *Genta et al*[84], lymphoid follicles were found in all patients with *Helicobacter pylori* infection but were absent in normal controls.

Wootherspoon et al(1991)[85] demonstrated that the lymphoid tissue seen in *Helicobacter pylori* infected stomachs had all the morphological features of MALT.

Wotherspoon and co-workers(1993)[86] observed the effect of eradication of the organism on a small series of early lymphomas . They found tumour regression in 5/6 cases treated by *Helicobacter pylori* eradication alone.

Bayerdorffer E et al(1995), Stolte M et al(1996), Montalban C et al (1996),Zucca E et al(1996), in their subsequent studies supported the suggestion that eradication of *Helicobacter pylori* can induce tumour regression in the absence of any other therapy[87-90].

DIABETES MELLITUS, DYSPEPSIA AND HELICOBACTER PYLORI

Diabetic patients often suffer from symptoms arising from the gastrointestinal apparatus[91-93]. The first report on gastric abnormalities occuring in diabetic subjects was published in 1945.[94]

Nevertheless, much later it's principal clinical expression, the so called 'gastroparesis diabeticorum', was described and it's association with the autonomic neuropathy recognised [95]. Subjects suffering from gastro-enteric abnormalities may be completely asymptomatic or affected only by a generical dyspepsia [96,97].

In addition to autonomic neuropathy, other factors may also be considered causative of esophageal or gastric dysfunctions - abnormalities of the esophageal and/or gastric motility

1. Direct effect of hypoglycemia and hyperinsulinemia [98] on gastro-enteric motility[99].

2. Altered production of gastrointestinal hormones, related or not to autonomic neuropathy [91,96,100].

3. Susceptibility to infectious diseases frequently observed in patients with an unsatisfactory metabolic control [97,101].

Talley NJ (1993),Lambert JR (1993), Dooley C.P et al (1989), Bernerson B. et al(1992) in their different studies found prevalence of Helicobacter pylori infection to be 50% in patients affected by non-ulcer dyspepsia (51,102-104).

Qvist. N. et al (1994) found prevalence of Helicobacter pylori infection to reach up to 76% when concomitant abnormalities of gastro-enteric motility were present [105].

Few and controversial data are available, so far, on the prevalence of Helicobacter pylori in diabetic patients [106-108]. *De Caprio, M., et al (1994)* reported a higher prevalence of *Helicobacter pylori* in a series of symptomatic and asymptomatic type 2 diabetic patients [106-108].

Kojeccky et al.(1993) described no significant difference between 91 NIDDM unselected patients (affected by dyspepsia, gastritis, gastric and/or duodenal ulcer) and comparable non-diabetic subjects[107].

Malecki M, Bien AI, et al (1996), based on histological demonstration of the presense of *Helicobacter pylori* stated the prevalence of infection to be lower in patients with diabetes than in controls [109].

Gasbarrini G, et al(1998), Chia-Hung K, et al (1995), based on C-13 Urea breath test ,reported a similar prevalence in patients with diabetes and controls of same age[110,111].

The study of *Oldenburg et al (1996)*, based on serologic antibody determinations, indicated a higher prevalence in patients with diabetes than in controls in nearly all of their age-based subgroups [112].

AU Morollo M et al (2001), in their study showed a higher prevalence of *Helicobacter pylori* infection in diabetes mellitus patients with dyspepsia. *Helicobacter pylori* infection was significantly associated with presence of endoscopic lesions and chronic gastritis in diabetic patients, but not in controls.[113]

AU Quatrini M et al (2001) also found higher prevalence of *Helicobacter pylori* infection, esophagitis and peptic ulcer in their patients with diabetes (with or without dyspepsia) suggesting that diabetics should be considered at risk for *Helicobacter pylori* infection and are suitable candidates for treatment.[114]

Persico M et al (1996) in their study also documented higher prevalence of *Helicobacter pylori* infection in patients affected by type 2 diabetes and non-ulcer dyspepsia with a significant higher prevalence in subjects with autonomic neuropathy.[115]

Zelenkova J et al (2002) in their study showed a lower seroprevalence of *Helicobacter pylori* in diabetic patients of type I and II in comparison with the healthy population[116]

Sato T et al (2002) also showed higher prevalence of peptic ulcer disease in asymptomatic diabetic patients and suggested that the eradication of *Helicobacter pylori* becomes the first therapy in peptic ulcer patients with non-insulin dependent diabetes mellitus. [117]

Ko GT, Chan FK et al (2001) found the rate of *Helicobacter pylori* infection in Hong Kong Chinese subjects with type 2 diabetes to be around 50%, which was similar to control subjects. No association was found between *Helicobacter pylori* infection, glycaemic status, and duration of diabetes and upper gastrointestinal symptoms in these diabetic subjects.[118]

Ojetti V, Pitocco D et al (2001) observed a significantly higher incidence of *Helicobacter pylori* re-infection in IDDM patients when compared to non IDDM controls [119].

Guvener N, Akcan Y (1999) in their study concluded that the prevalence of *Heliccobacter pylori* gastritis is higher in asymptomatic diabetic patients compared with healthy people. But they found no association between the alterations in GET and the presence of *Helicobacter pylori* gastritis as indicated.[120]

Gasbarrini A, Ojetti V et al (1999) observed that IDDM patients showed a significantly lower *Helicobacter pylori* eradication rate when compared to that observed in dyspeptic subjects. The impairment of the

gastrointestinal mucosa microvasculature with a reduction of antibiotic absorption may be the mechanisms underlying the observation[121].

Gentile S, Turco S et al (1998) for the first time, provided direct evidence for a higher frequency of *Helicobacter pylori* infection in dyspeptic patients affected with DM2 than in non-diabetic subjects and associated it with autonomic neuropathy.[122],

MATERIAL & METHODS

MATERIAL AND METHODS

The present study was conducted in the Gastroenterology section, Department of Medicine, M.L.B. Medical College Jhansi, in active collaboration with the Department of Pathology, M.L.B.Medical College, and Jhansi.

A. Selection of study group

Study group was constituted by the diabetic (NIDDM) and non-diabetic(controls) dyspeptic patients attending medicine in and out patient department of all age groups belonging to different strata of society who agreed to undergo upper gastrointestinal endoscopy.

Dyspepsia being defined as nausea, bloating, sour eructation, early satiety, heart burn or epigastric discomfort for at least one month.

The following exclusion criteria were applied in both diabetic and non-diabetic dyspeptic patient groups.

1. Treatment during previous month with gastroerosive medications, antibiotics , proton pump inhibitors or NSAIDS corticostericids bismuth derived drugs .

2. Patients who received anti H. pylori treatment before.

3. The patients with cholelithiasis, previous cholecystectomy, or major gastrointestinal surgery were excluded.

B. Clinical evaluation of patients / subjects

The detailed history including age, sex, occupation, socio-economic status, total duration of illness, any treatment received was taken.

A physical examination to assess the general condition (pulse rate, blood pressure, pallor, icterus, edema , lymph node enlargement , cyanosis and clubbing) was carried out.

The presence of autonomic neuropathy was evaluated using standard test (postural hypotension, hand grip test).

Postural hypotension defined as sustained drops in systolic (> 20 mm Hg) or diastolic (> 10 mm Hg) BP after standing from supine position for at least 2 min that are not associated with an increase in pulse rate of > 15 beats per minute.

Hand grip test – patient was asked to make a sustained tight handgrip for 5 min. This act normally increases the heart rate and the systolic and diastolic pressures by 15 mm Hg or more. The reduced or absent response was considered to indicate autonomic neuropathy.

General investigations like Hemogram, Blood sugar, BT,CT, Boold Urea , Serum creatinine were done before subjecting patients to biopsy.

C. Procedure

The invasive tests including endoscopy followed by antrum biopsy were done .

ENDOSCOPY AND BIOPSY

a) Prepration for Endoscopy:

1. All patient were examined thoroughly to exclude other systemic disease.

2. All patients were asked for overnight fasting and endoscopy was performed in morning.

3. Every patient was explained about the procedure and given reassurance.

4. End viewing flexible OLYMPUS (model GIF 10Q.) fibreoptic oesophagogastroduodenoscope was used. Proper consent was taken before each endoscopic procedure.

5. To facilitate the passage of instrument oropharyngeal anaesthesia was achieved with 2% Xylocaine gargle and lubricating jelly was applied on the tube.

b) Position of Patient:

Patient was placed in left lateral decubitus position with a single pillow under patient's head. An assistant placed a mouth gag in position and controlled the patient's head.

c) Procedure:

Endoscope was placed in oropharynx and patient was asked to assist passage by making swallowing movement. After passing the cricopharynx the tip was further guided forward under direct vision. Air insufflation and suction were done as required. The oesophagus, stomach and duodenum were examined carefully during passing endoscope as well as during withdrawing the instrument.

The biopsy forceps were sterilized after each patient by soaking in a 2% solution of gluteraldehyde (Cidex) and allowing them to dry. They were rinsed in tap water before the first biopsy specimen was taken.

Three antral biopsy specimens were taken from each patient, the first one for rapid urease test and two other for histopathological studies. Biopsy specimens were taken from mucosa 5 cm of the pylorus, one histology specimen from the greater curve and the other from the lesser curve. It was not necessary to obtain red mucosa to demonstrate either bacteria or gastritis.

DIAGNOSIS OF H. PYLORI INFECTION

The biopsy specimen were then subjected to :

1 Rapid urease test.

2. Histological demonstration of the organism.

1. RAPID UREASE TEST:

Heliobacter pylori has a very high endogenous urease activity and split urea rapidly by the action of enzyme urease forming ammonia which causes change in pH (i.e) towards alkaline). This change in pH is indicated by appearance of intense pink red colour.

Rapid urease solution :

Ingredients	In gms/ liter purified Filtered water
Urea	20.0
Mono sodium phosphade	0.7
Phenol red	0.1
Agar	4.0

pH= 6.4± 0.2at 25^{0}C

Storage:

The prepared media was stored at 2-8^{0}C away from direct light.

Specimen Collection

Biopsy specimen from antrum is placed directly into rapid urease medium at the time of endoscopy.

Method of use

Biopsy specimen was submerged in the medium, the inoculated tube was incubated aerobically at room temperature for up to 20 hours to 3 days. Colour change usually occurs within 4 hours but can occur upto 24 hours. Colour change from yellow to pink indicates presence of H. pylori.

Interpretation.

Positive: Intense pink (red – violet) colour.

Negative: No Colour change (yellow).

False reaction:

Can be given by proteus species which are also capable of splitting urea at a much slower rate.

False –negative findings

The possible causes of false negative findings are listed as follows

Endoscopy

- Lignocaine swallowed
- Simethicone given before biopsy

- Patient taking bismuth preparations or antibiotic drugs.
- Cimetidine or ranitidine tablets in the stomach.
- Biopsy forceps contaminated with gluteraldehyde.
- Biopsy specimen containing no antral epithelium.

Histology

- Specimen containing mainly intestinal metaplasia.
- Specimen containing mainly acid secreting mucosa.
- Low number of bacteria and poor Silver stain.

2. HISTOLOGY:

Biopsy specimen from antrum, preserved in formalin is sent to Department of Pathology for direct visualization / demonstration of Helicobacter pylori and other histological additional information including the degree and pattern of inflammation, atrophy , metaplasia and dysplasia in Giemsa staining.

3. ENDOSCOPIC FINDINGS

Endoscopic findings were assessed in the following headings- Reflux esophagitis/ gastritis/gastric ulcer/duodenal ulcer / duodenitis /malignancy/normal findings.

OBSERVATIONS

OBSERVATIONS

A total of 63 dyspeptic patients attending the out patient department and admitted in the hospital were studied . Out of which 25 patients were diabetic and 38 patients were non diabetic (control group)

The two groups were compared under the following headings-

1. Findings following Rapid urease test
2. Findings of histo-pathological examination in RUT negative patients
3. *H. Pylori* status in diabetics and non diabetics
4. Age
5. Sex
6. Socio economic status
7. Locality
8. Presenting symptoms
9. Duration of complaints
10. Duration of diabetes
11. Findings of upper G.I endoscopy
12. Prevalence of autonomic neuropathy in *H. pylori* positive and negative patients.

1.RAPID UREASE TEST

Table 1 presents distribution of cases according to findings following RUT

TABLE-1

DISTRIBUTION OF CASES ACCORDING TO FINDINGS FOLLOWING RUT:-

Rapid urease test(RUT)	Diabetics dyspeptics	Control dyspeptics
RUT+ve	18(72%)	20(52.6%)
RUT-ve	7(28%)	18(47.4%)
Total cases	25	38

The entire study was conducted by dividing the cases in two groups diabetic and control dyspeptics. Among the 20 diabetic dyspeptics, 18 patients were RUT+ve (72% of diabetic dyspeptics) while 7 were RUT-ve (28% of diabetic dyspeptics).

Among control dyspeptics 20 cases (52.6% of control dyspeptic) were RUT+ve while 18 cases (47.4% of control dyspeptic) were RUT-ve.

2.HISTO-PATHOLOGICAL EXAMINATION

Table 2 presents distribution of cases according to findings following histo-pathological examination in RUT-ve cases

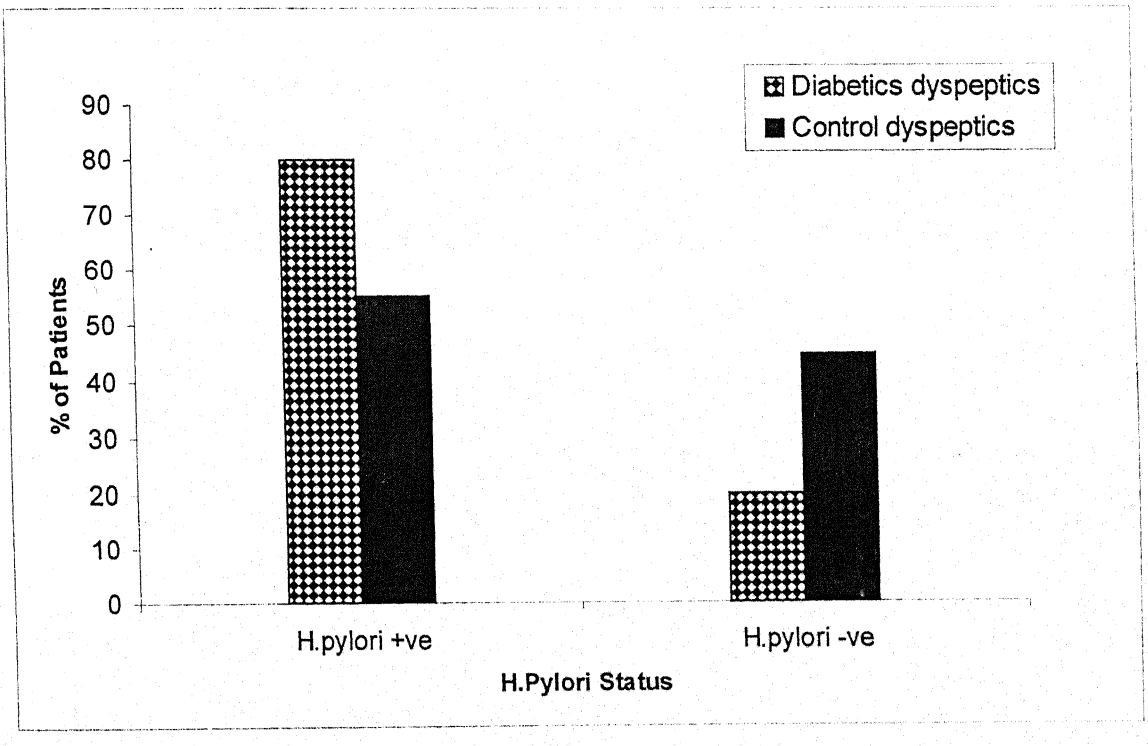
TABLE-2

DISTRIBUTION OF CASES ACCORDING TO FINDINGS FOLLOWING HISTO-PATHOLOGICAL EXAMINATION IN RUT-VE CASES;-

Histopathological examination	Diabetics dyspeptics	Control dyspeptics
H.pylori colonies +nt	2	1
H.pylori colonies -nt	5	17
Total RUT-ve cases	7	18

Of the 7 RUT –ve diabetic dyspeptics, 2 patient were *H.pylori* +ve following histopathological examination. Of the 18 RUT –ve control dyspeptics 1 patient was *H.pylori* +ve following histopathological examination.

DISTRIBUTION OF CASES ACCORDING TO H.PYLORI STATUS



3. *H.PYLORI* STATUS

Table 3 presents distribution of cases according to *H.pylori* status

TABLE-3

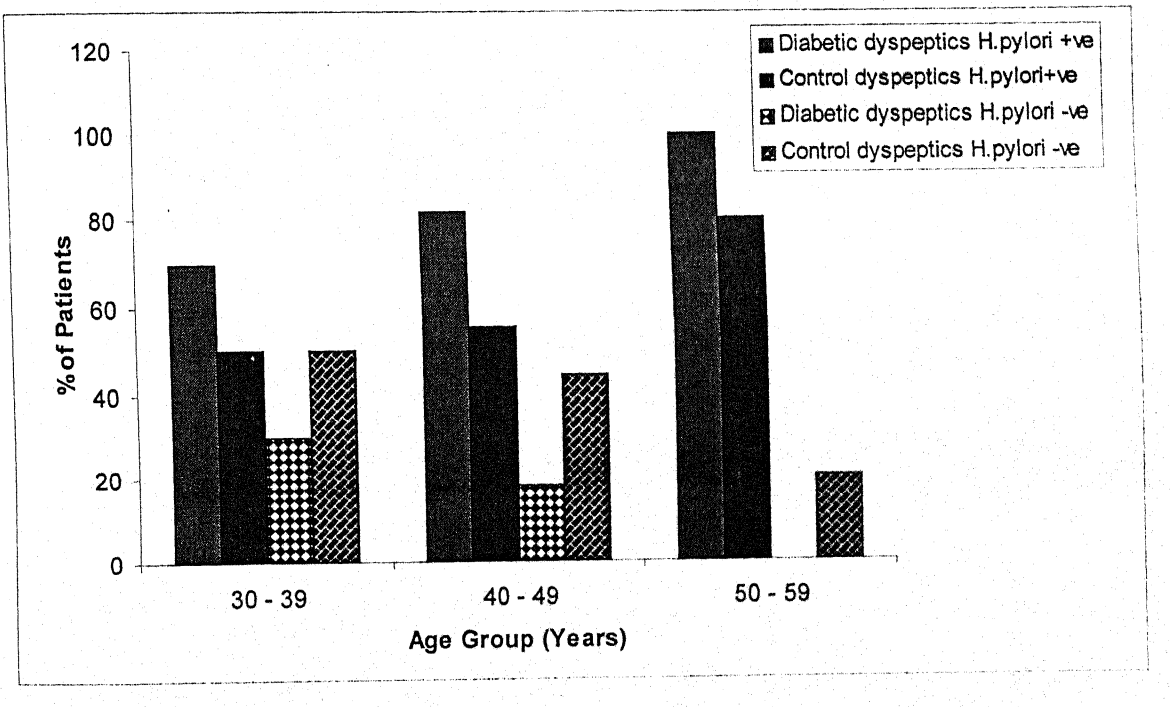
DISTIBUTION OF CASES ACCORDING TO H.PYLORI STATUS:-

H.pylori status	Diabetic dyspeptics	Control dyspeptics
H.pylori +ve	20(80%)	21(55.26%)
H.pylori -ve	5(20%)	17(44.74%)
Total cases	25	38

P value < 0.05; significant

Thus a total of 20 out of 25 diabetic dyspeptics patients were H.pylori +ve (80%) and a total of 21 out of 38 control dyspeptics patients were H.pylori +ve (55.26%).

DISTRIBUTION OF CASES ACCORDING TO AGE



4. AGE

Table 4 presents distribution of cases according to age group

TABLE-4

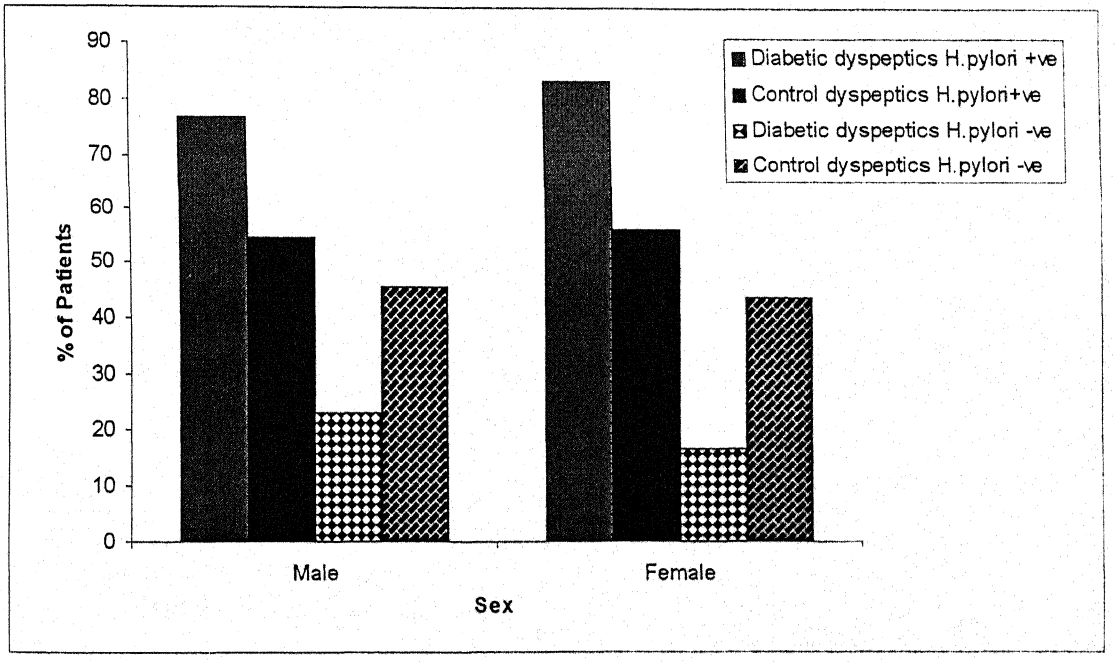
DISTRIBUTION OF CASES ACCORDING TO AGE GROUP

Age group in yrs	Diabetic dyspeptics			Control dyspeptics		
	H.pylori +ve	*H.pylori* -ve	Total	*H.pylori* +ve	*H.pylori* - ve	Total
30-39	7(70%)	3(30%)	10	12(50%)	12(50%)	24
40-49	9(81.8%)	2(18.2%)	11	5(55.5%)	4(44.4%)	9
50-59	4(100%)	-	4	4(80%)	1(20%)	5
>60	-	-	-	-	-	-

P value > 0.1;not significant

In the age group 30-39 years, there were 10 diabetic dyspeptic patients among which 7(70%) were *H.pylori* +ve and 3 (30%) were *H.pylori* -ve and there were 24 control dyspeptics in this group, among which 12(50%) were *H.pylori* +ve and 12(50%) were *H.pylori* -ve. In 40-49 years age group, there were 11 diabetic dyspeptic of which 9 (81.8%) were *H.pylori* +ve and 2(18.2%) were *H.pylori* -ve. Among control dyspeptics, there were 9 patients in this age group ,of which 5(55.5%) were *H.pylori* +ve and 4(44.4%) were *H.pylori* -ve. In the 50-

DISTRIBUTION OF CASES ACCORDING TO SEX



59 age group . there were only 4 diabetic dyspeptic patients, all(100%) were *H.pylori* +ve. Among control dyspeptics, a total of 5 patients were there in this age group with 4(80%) being *H.pylori* +ve and 1(20%) being *H.pylori* -ve. In age group >60 years, there were no diabetic or control dyspeptic patients.

5. SEX

Table 5 presents distribution of cases according to sex

TABLE-5

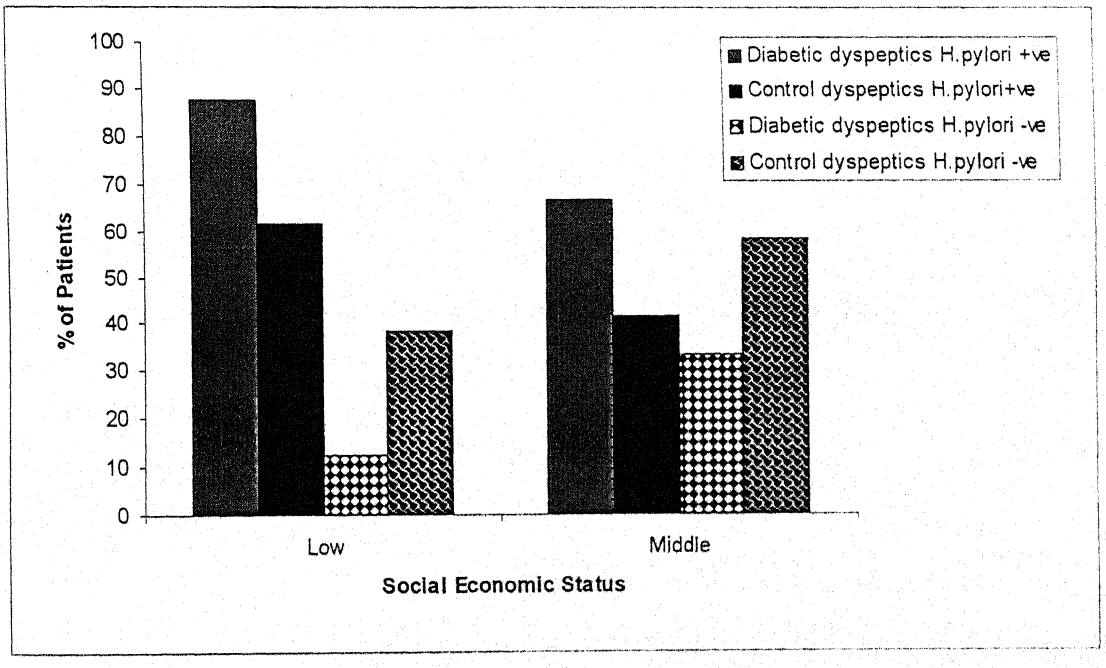
DISTRIBUTION OF CASES ACCORDING TO SEX

SEX	Diabetic dyspeptics			Control dyspeptics		
	H.pylori +ve	*H.pylori* –ve	*Total*	*H.pylori* +ve	*H.pylori* -ve	*Total*
Male	10 (76.9%)	3 (23.1%)	13	12 (54.5%)	10 (45.5%)	22
Female	10 (83.3%)	2 (16.7%)	12	9 (56.25%)	7 (43.75%)	16

P value > 0.1;not significant

Among diabetic dyspeptics, 13(52%) patients were male with 10(76.9%) patients *H.pylori* +ve and 3(23.1%) patients *H.pylori* -ve. In controls dyspeptic 22(57.9%) patients were male with 12(54.5% *H.pylori* +ve and 10(45.5%) patients *H.pylori* -ve. A total of 12(48%)

DISTRIBUTION OF CASES ACCORDING TO SOCIO ECONOMIC STATUS



female patients were there in the diabetic dyspeptic group with 10(83.3%) being *H.pylori* +ve and 2(16.7%) being *H.pylori* -ve. A total of 16(42.1%) females were there in the control dyspeptic group with 9(56.25%) *H.pylori* +ve and 7(43.75%) being *H.pylori* –ve patients.

6. SOCIO ECONOMIC STATUS

Table 6 presents distribution of cases according to socio economic status

TABLE-6

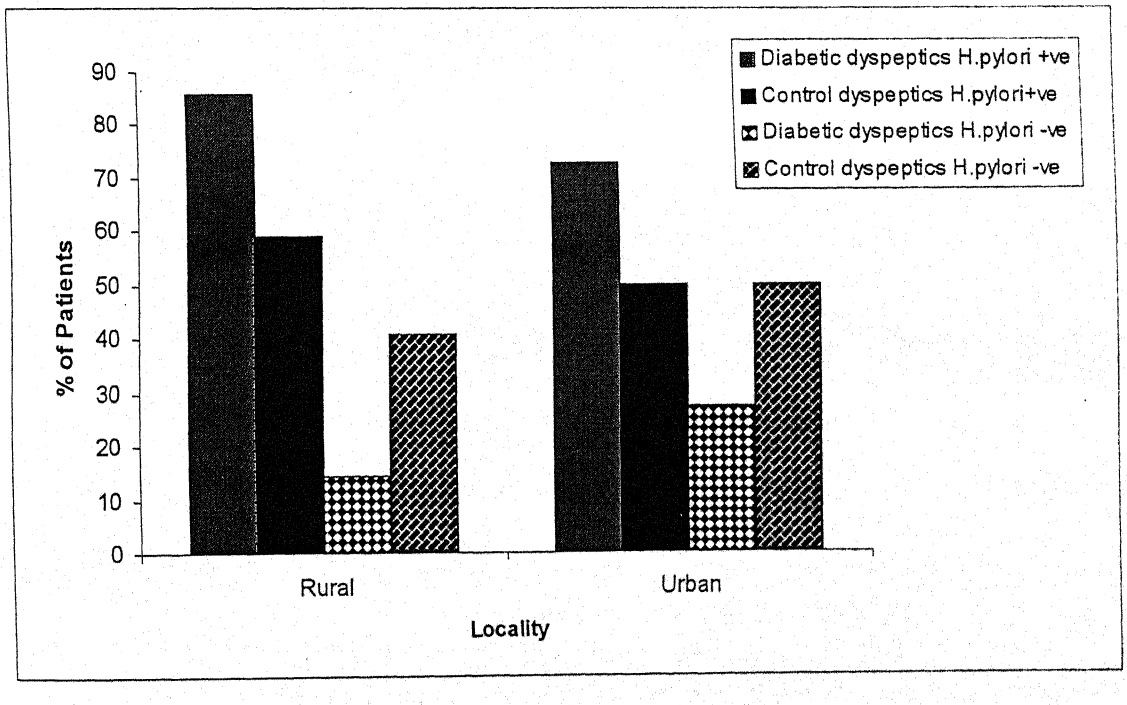
DISTRIBUTION OF CASES ACCORDING TO SOCIO ECONOMIC STATUS

Socioeconomic status	Diabetic dyspeptics			Control dyspeptics		
	H.pylori +ve	*H.pylori* -ve	Total	*H.pylori* +ve	*H.pylori* -ve	Total
Low	14 (87.5%)	2 (12.5%)	16	16 (61.5%)	10 (38.5%)	26
Middle	6 (66.7%)	3 (33.3%)	9	5 (41.7%)	7 (58.3%)	12
High	-	-	-	-	-	-

P value > 0.1;not significant

In the diabetic dyspeptic group, a total of 16(64%) patients belonged to the low socioeconomic status, of which 14(87.5%)were *H.pylori* +ve patients and 2(12.5%) were *H.pylori* -ve. Among the control dyspeptics, a total of 26(68.4%) patients were in the low socioeconomic group of which 16(61.5%) were *H.pylori* +ve and 10(38.5%)were *H.pylori* -ve. A total of 9(36%) diabetic dyspeptic patients belonged to middle socioeconomic group with 6(66.66%) being *H.pylori* +ve and 3(33.33%) patients being *H.pylori* -ve. Among control dyspeptics, 12(31.58%) patients belonged to middle socioeconomic group of which 5(41.7%) were *H.pylori* +ve and 7(58.3%) were *H.pylori -ve*.

DISTRIBUTION OF CASES ACCORDING TO LOCALITY



7. LOCALITIES

Table 7 presents distribution of cases according to rural or urban localities

TABLE-7

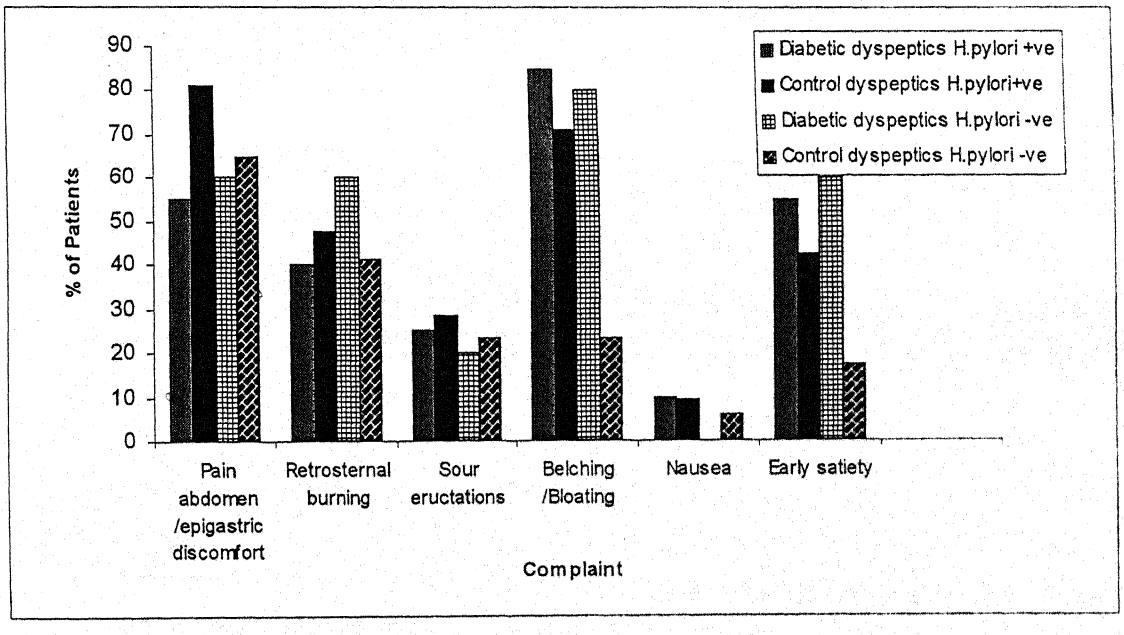
DISTRIBUTION OF CASES ACCORDING TO RURAL OR URBAN LOCALITIES

Locality	Diabetic dyspeptics			Control dyspeptics		
	H.pylori +ve	*H.pylori* -ve	Total	*H.pylori* +ve	*H.pylori* -ve	Total
Rural	12(85.7%)	2(14.3%)	14	13(59.1%)	9(40.9%)	22
Urban	8(72.7%)	3(27.3%)	11	8(50%)	8(50%)	16

P value > 0.1;not significant

A total of 14 (56%) diabetics dyspeptic patients were from rural areas of which 12(85.7%) were *H.pylori* +ve and 2(14.3%) were *H.pylori* -ve and in control dyspeptics 22(57.9%)patients were from rural area with 13(59.1%) *H.pylori* +ve patients and 9(40.9%) *H.pylori* -ve patients. A total of 11(44%) diabetic dyspeptic patients came from urban areas with 8(72.7%) *H.pylori* +ve and 3(27.3%) patients *H.pylori* -ve. In controls, 16(42.1%) patients were from urban areas with 8(50%) *H.pylori* +ve and 8(50%) patients *H.pylori* -ve.

DISTRIBUTION OF CASES ACCORDING TO PRESENTING COMPLAINTS



8. PRESENTING SYMPTOMS

Table 8 presents distribution of cases according to presenting complaints.

TABLE-8

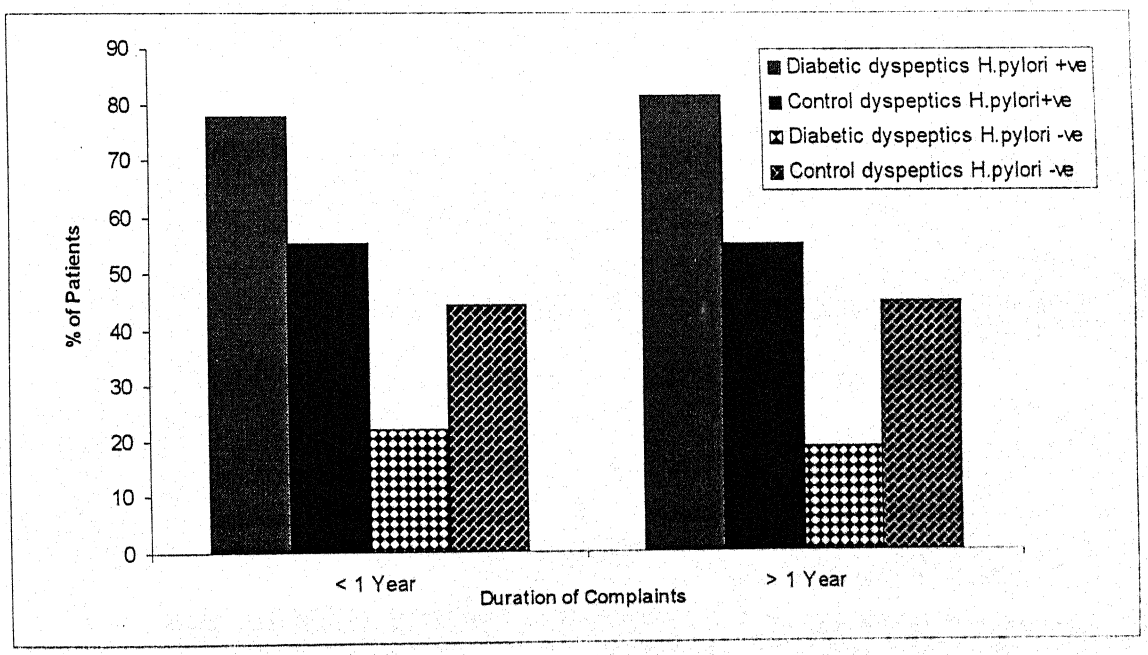
DISTRIBUTION OF CASES ACCORDING TO PRESENTING COMPLAINTS

Complaints	Diabetic dyspeptics			Control dyspeptics		
	H.pylori +ve	*H.pylori* -ve	Total	*H.pylori* +ve	*H.pylori* - ve	Total
Pain abdomen /epigastric discomfort	11(55%)	3(60%)	14	17(81%)	11(64.7%)	28
Retrosternal burning	8(40%)	3(60%)	11	10(47.6%)	7(41.18%)	17
Sour eructations	5(25%)	1(20%)	6	6(28.6%)	4(23.5%)	10
Belching /Bloating	17(85%)	4(80%)	21	15(71.4%)	4(23.5%)	19
Nausea	2(10 %)	-	2	2(9.5%)	1(5.88%)	13
Early satiety	11(55%)	3(60%)	14	9(42.85%)	3(17.65%)	12

Among diabetic dyspeptics, the most common complaint was belching /bloating seen in 21(84%) patients , of which 17(85%) of *H.pylori* +ve diabetic dyspeptic) were *H.pylori* +ve and 4(80%) of *H.pylori* -ve diabetic dyspeptic) were *H.pylori* -ve, which is almost equal . The second most common complaints were pain in abdomen /epigastric discomfort and early satiety seen in 14(56%) patients. 11 *H.pylori* +ve patients(55% of *H.pylori* +ve diabetic dyspeptics) and 3 *H.pylori* -ve patients (60% of *H.pylori* -ve diabetic dyspeptics) had pain in abdomen /epigastric discomfort while 11 *H.pylori* +ve patients (55% of *H.pylori* +ve diabetic dyspeptics) and 3 *H.pylori* -ve patients (60% of *H.pylori* -ve diabetic dyspeptics) had the complaints of early satiety .

Among controls, the most common complaint was pain in abdomen / epigastric discomfort seen in 28(73.7%) patients with 17(81% of *H.pylori* +ve control dyspeptics) being *H.pylori* +ve and 11(64.7% of *H.pylori* -ve control dyspeptic) being *H.pylori* -ve. The second most common complaint was belching found in 19(50%) patients of which 15(71.4% of *H.pylori* +ve control dyspeptics) were *H.pylori* +ve and 4(23.53% of *H.pylori* +ve control dyspeptics) patients were *H.pylori* -ve.

DISTRIBUTION OF CASES ACCORDING TO DURATION OF COMPLAINTS



9. DURATION OF COMPLAINTS

Table 9 presents distribution of cases according to duration of complaints

TABLE-9

DISTRIBUTION OF CASES ACCORDING TO DURATION OF COMPLAINTS:-

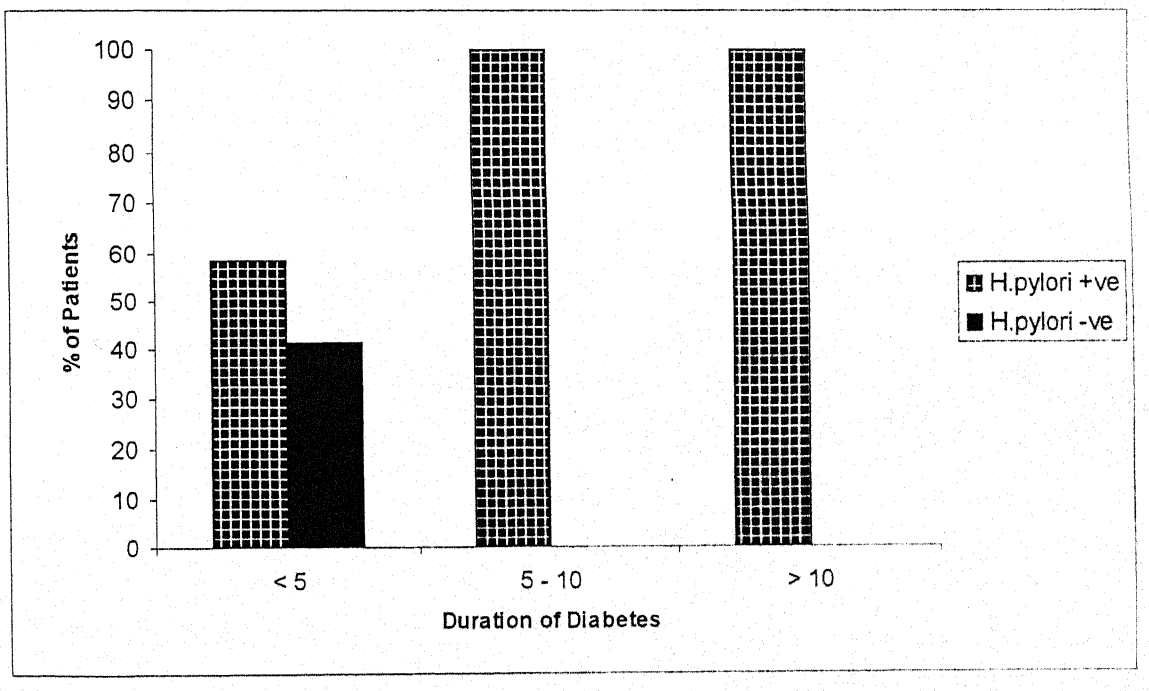
Duration of complaints	Diabetic dyspeptics			Control dyspeptics		
	H.pylori +ve	*H.pylori* -ve	Total	*H.pylori* +ve	*H.pylori* -ve	Total
<1 year	7(77.8%)	2(22.2%)	9	10(55.5%)	8(44.5%)	18
>1 year	13(81.25%)	3(18.75%)	16	11(55%)	9(45%)	20

P value > 0.1;not significant

Among diabetic dyspeptic 9(36%) patients, 7(77.8%) *H.pylori* +ve and 2(22.2%) *H.pylori* -ve had complaints for a duration <1 year, while among control dyspeptic a total of 18(47.4%) patient with 10(55.5%) *H.pylori* +ve and 8(44.5%) *H.pylori* -ve patients had symptoms for a duration <1 year.

Maximum no. of diabetic dyspeptics i.e. 16(64%) had symptoms for >1 year, of which 3(18.75%) were *H.pylori* +ve and 4(25%) were *H.pylori* –ve. Among control dyspeptics, maximum no. of patients i.e.

DISTRIBUTION OF CASES ACCORDING TO DURATION OF DIABETES



20(52.63%) patients had symptoms >1year with 11(55%) being *H.pylori* +ve and 9(45%) being *H.pylori* -ve.

10. DURATION OF DIABETES

Table 10 presents distribution of cases according to duration of diabetes

TABLE-10

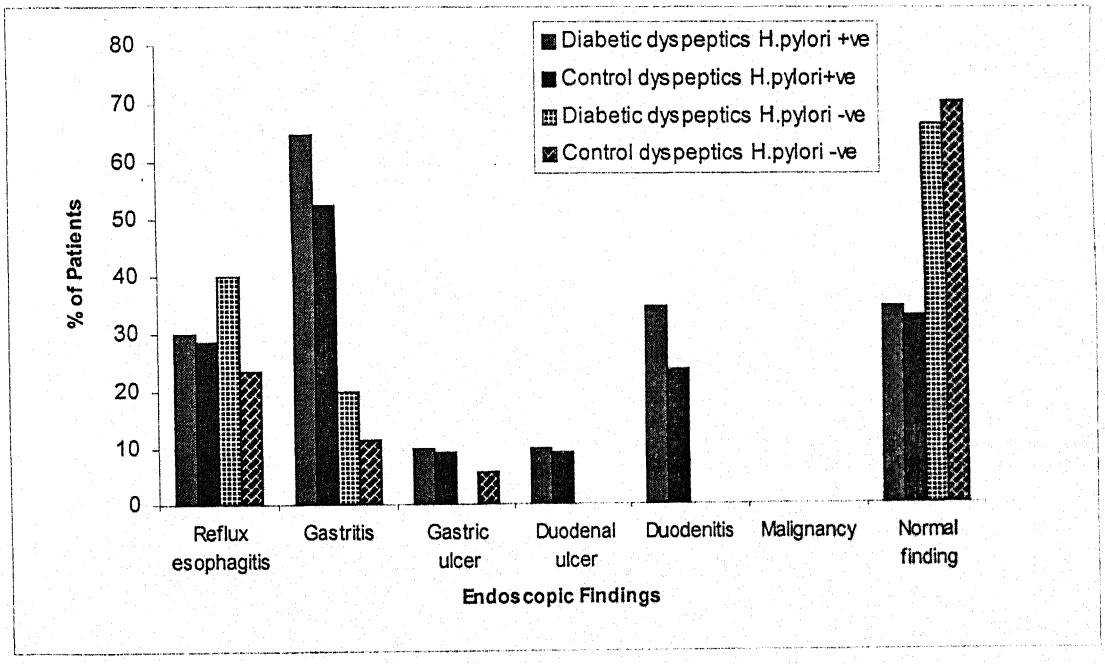
DISTRIBUTION OF CASES ACCORDING TO DURATION OF DIABETES

Duration of diabetes	Diabetic dyspeptics		
	H.pylori +ve	*H.pylori* -ve	Total
<5 years	7(58.3%)	5(41.7)	12
5-10 years	10(100%)	-	10
> 10 years	3(100%)	-	3

P value <0.05; significant

Among diabetic dyspeptic, max. no. of patients i.e. 12(48%) had diabetics detected < 5 years ago of which 7(58.3%) were *H.pylori* +ve, 5(41.7%) were *H.pylori* -ve. 10 (40%) patients had diabetes for a duration > 5 years,all (100%) were *H.pylori* +ve. 3(12%) diabetic dyspeptics had diabetes detected for > 10 years, all were *H.pylori* +ve.

DISTRIBUTION OF CASES ACCORDING TO UPPER G.I. ENDOSCOPIC FINDINGS



11. FINDINGS OF UPPER GI ENDOSCOPY

Table 11 presents distribution of cases according to findings of upper GI endoscopy

TABLE-11

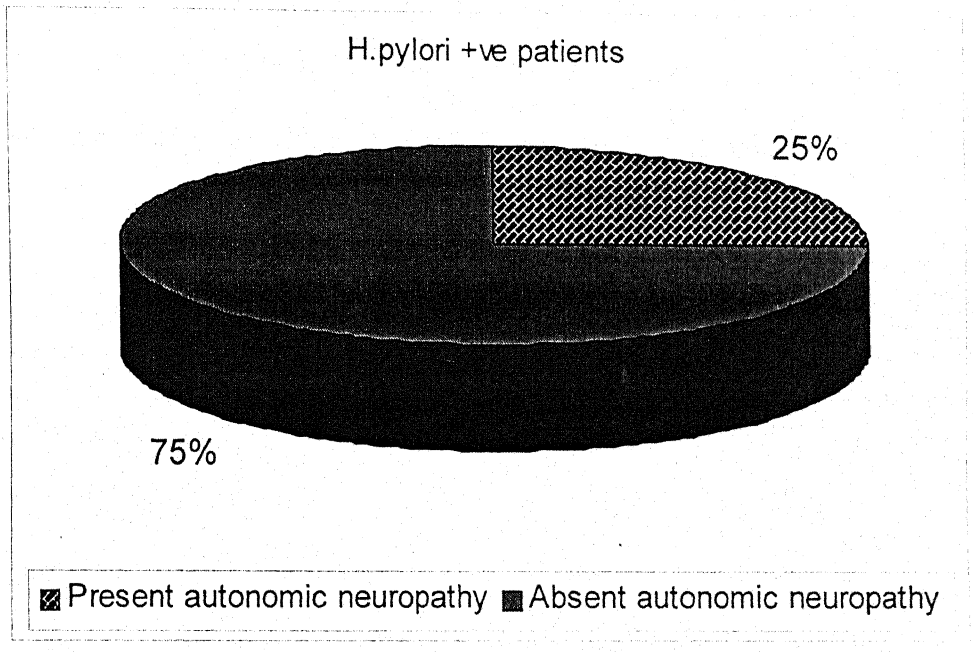
DISTRIBUTION OF CASES ACCORDING TO FINDINGS OF UPPER GI ENDOSCOPY

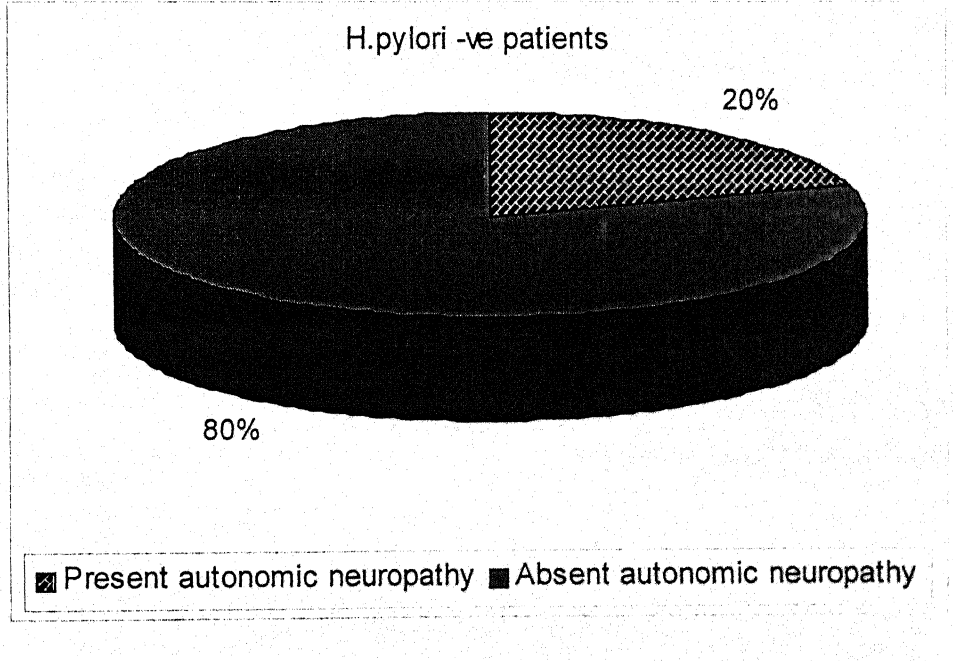
Endoscopic finding	Diabetic dyspeptics			Control dyspeptics		
	H.pylori +ve	*H.pylori* -ve	Tota	*H.pylori* +ve	*H.pylori* -ve	Total
Reflux esophagitis	6 (30%)	2 (40%)	8	6 (28.6%)	4 (23.5%)	10
Gastritis	13 (65%)	1 (20%)	14	11 (52.5%)	2 (11.76%)	13
Gastric ulcer	2 (10%)	-	2	2 (9.5%)	1 (5.88%)	2
Duodenal ulcer	2 (10%)	-	2	2 (9.5%)	-	2
Duodenitis	7 (35%)	-	7	5 (23.8%)	-	5
Malignancy	-	-	-	-	-	-
Normal finding	7 (35%)	3 (66.7%)	10	7 (33.3%)	12 (70.6%)	19

Among *H.pylori* +ve diabetic dyspeptics, upper G.I endoscopy finding was normal in 7 patients (35% of H.pylori +ve diabetic dyspeptic), gastritis in 13(65% of *H.pylori* +ve diabetic dyspeptics). Reflux esophagitis in 6 cases (30% of *H.pylori* +ve diabetic dyspeptics) in 2 cases (10% of *H.pylori* +ve diabetic dyspeptics) gastric ulcer, duodenitis in 7 cases (35% of *H.pylori* +ve diabetic dyspeptics), duodenal ulcer in 2 cases(10% of *H.pylori* +ve diabetic dyspeptics) was found. In the *H.pylori* +ve control dyspeptics normal findings in upper G.I endoscopy was seen in 7 patients (33.33% of *H.pylori* +ve control dyspeptics), gastritis in 11(52.4% of *H.pylori* +ve control dyspeptics), reflux esophagitis in 6 patients (28.6% of *H.pylori* +ve control dyspeptics), duodenitis in 5(23.8% of *H.pylori* +ve control dyspeptics), duodenal ulcer in 2(9.5 % of *H.pylori* +ve control dyspeptics) , and gastric ulcer in 2(9.5% of *H.pylori* +ve control dyspeptics) patients after upper G.I endoscopy . The findings in the 2 groups were almost similar. In *H.pylori* -ve diabetic dyspeptics normal upper G.I endoscopy was present in 3 patients (60% of *H.pylori* -ve diabetic dyspeptics), reflux esophagitis in 2 pateints (40% of *H.pylori* -ve diabetic dyspeptics) and gastritis in 1(20% of *H.pylori* -ve diabetic dyspeptics)

In H.pylori -ve control dyspeptics normal upper G.I endoscopy finding was found in 12 pateint (70.59% of *H.pylori* -ve control dyspeptics), reflux esophagitis in 4 pateints (23.5% of *H.pylori* -ve control dyspeptics), 2 patients (11.76% of *H.pylori* -ve control

DISTRIBUTION OF CASES ACCORDING TO AUTONOMIC NEUROPATHY





dyspeptics) had gastritis & 1(5.8% of *H.pylori* -ve control dyspeptics) had gastric ulcer on upper G.I endoscopy . The difference between two groups was not significant.

12. PREVALENCE OF AUTONOMIC NEUROPATHY

Table 12 presents distribution of cases according to the prevalence of autonomic neuropathy in diabetic dyspeptic patients

TABLE-12

DISTRIBUTION OF CASES ACCORDING TO THE PREVALENCE OF AUTONOMIC NEUROPATHY IN DIABETIC DYSPEPTIC PATIENTS:-

Autonomic neuropathy	Diabetic dyspeptics		
	H.pylori +ve	*H.pylori* -ve	Total
Present	5(25%)	1(20%)	6
Absent	15(75%)	4(80%)	19
	20	5	

P value > 0.1;not significant

In our study among diabetic dyspeptics having autonomic neuropathy 5(25%) patients were H.pylori +ve whereas 1(20%)was H.pylori –ve. The difference was not significant.

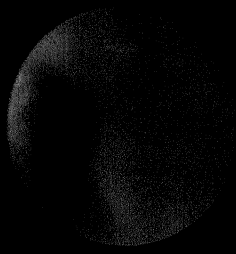


Figure -1. Endoscopic view of normal distal esophagus. Normal squamocolumnar junction is seen.

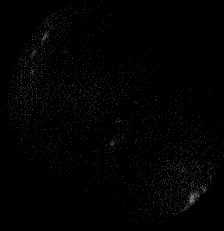


Figure-2 Normal rugal folds in the body of the stomach.

Figure-3. Normal antrum and angularis. There are no rugal folds.

Figure-4 . Normal descending doudenum, with the transverse folds of kerckring clearly evident.

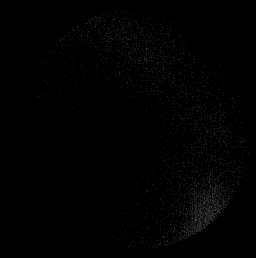


Figure-5a Hiatus hernia with reflux esophagitis.

Figure-5b Hiatus hernia with reflux esophagitis.

Figure-6a Gastrodudenitis . The mucosa is erythematous, with small superficial erosions.

Figure-6b Gastrodudenitis . The mucosa is erythematous, with small superficial erosions.

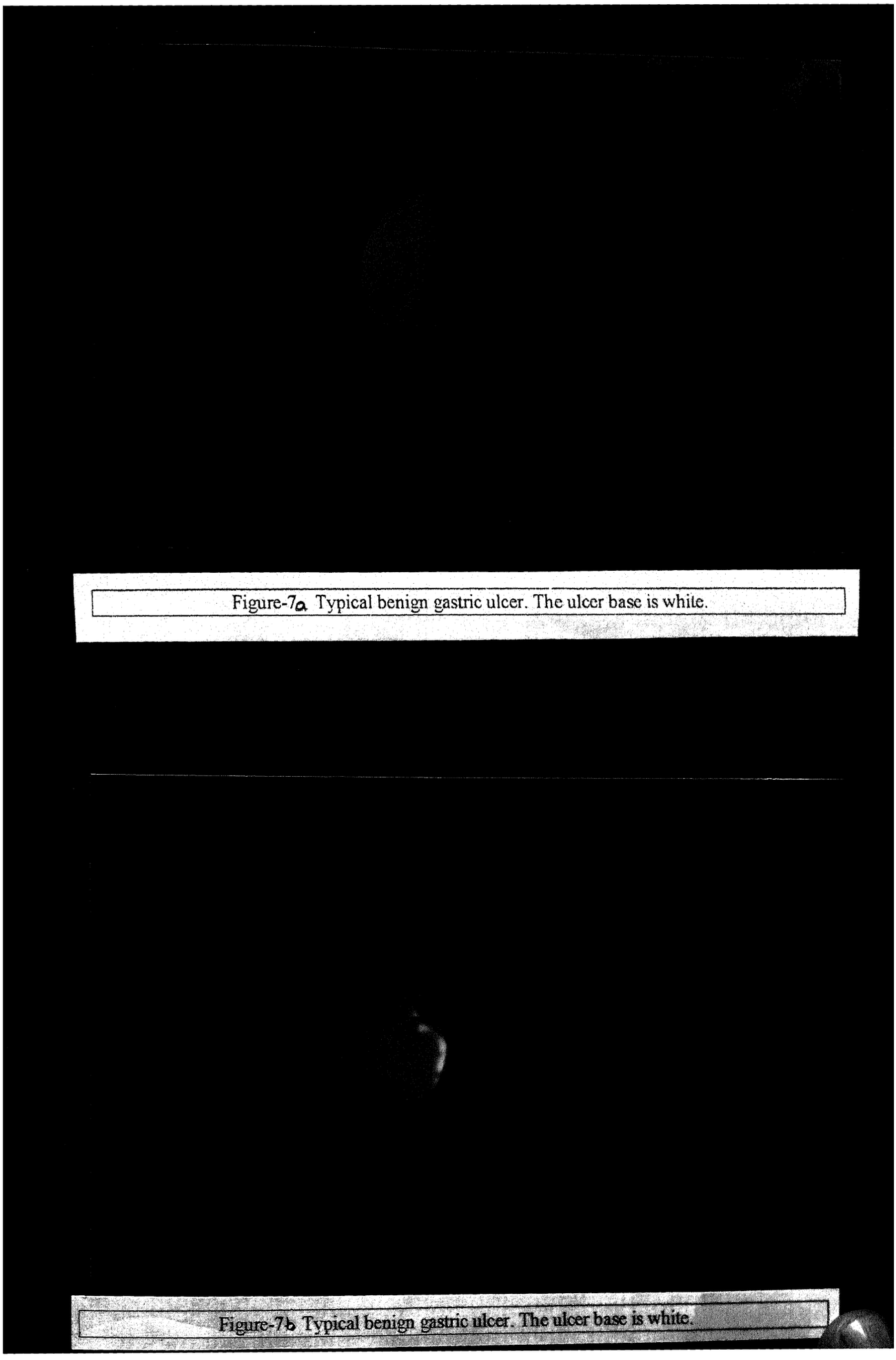


Figure-7a Typical benign gastric ulcer. The ulcer base is white.

Figure-7b Typical benign gastric ulcer. The ulcer base is white.

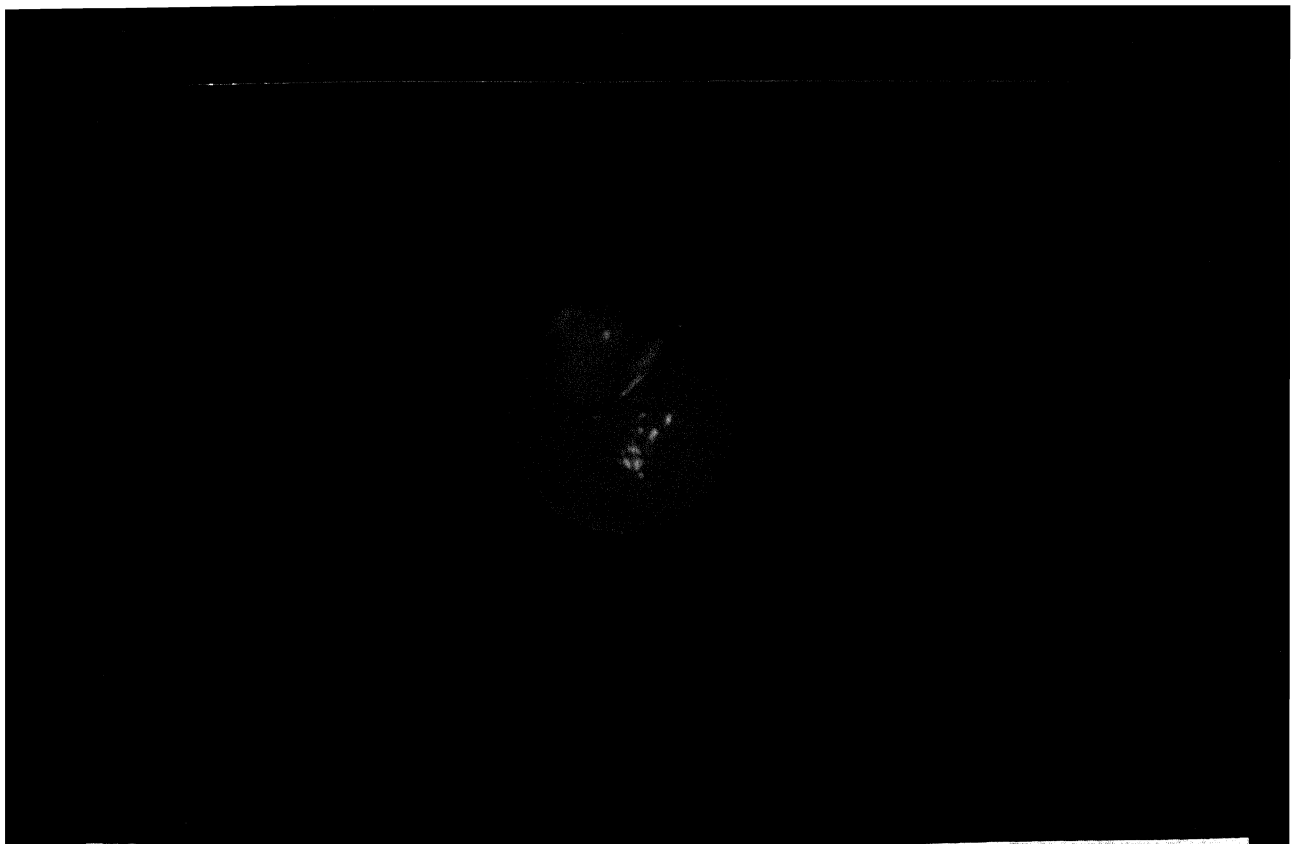


Figure-8a Large duodenal ulcer, extending from duodenal bulb to descending duodenum.

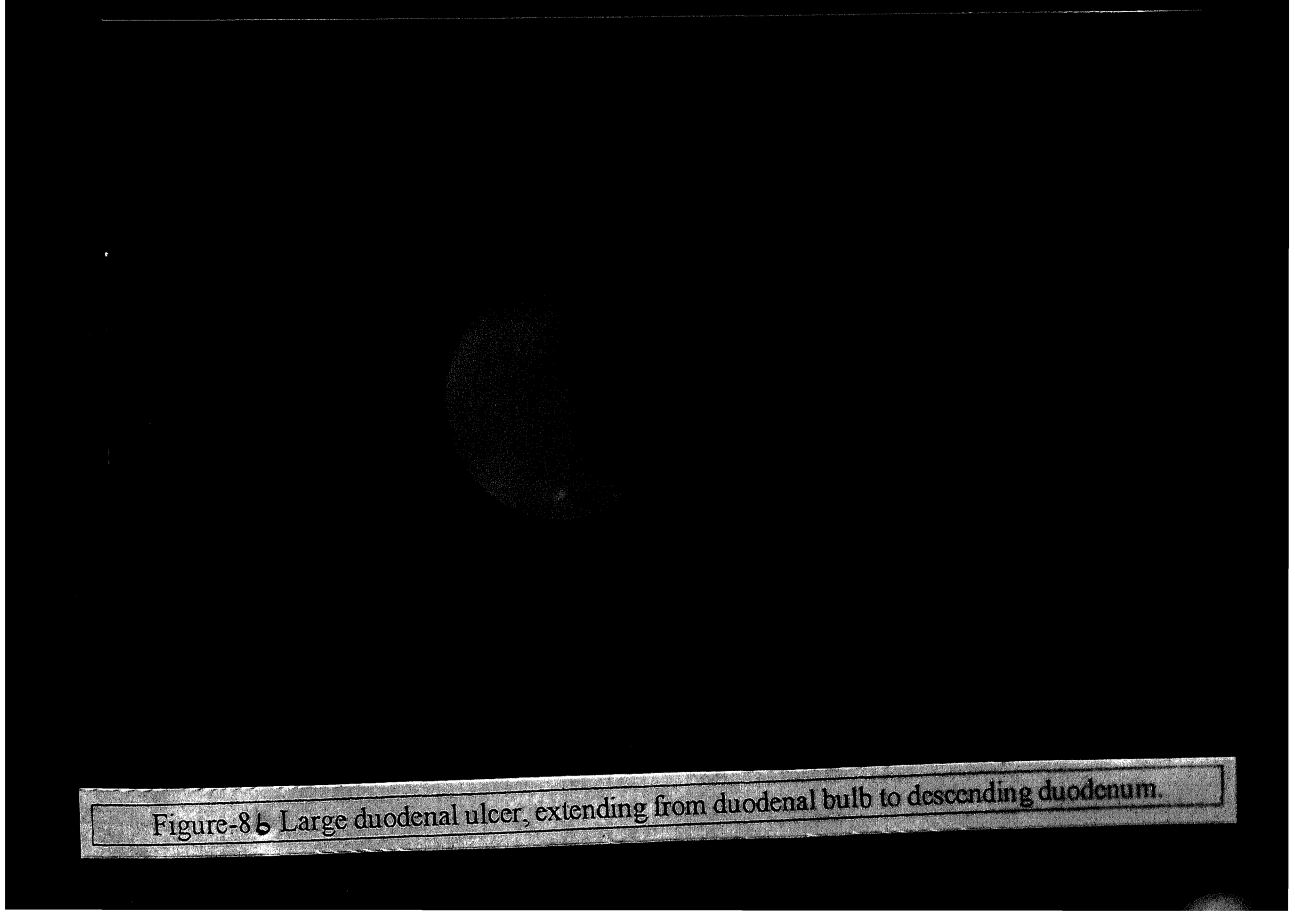


Figure-8b Large duodenal ulcer, extending from duodenal bulb to descending duodenum.

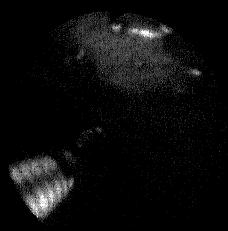


Figure-9a Biopsy specimen is being taken from antral mucosa.

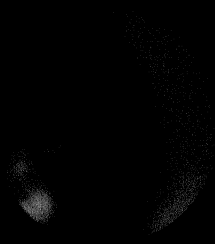


Figure-9b Biopsy specimen is being taken from antral mucosa.

DISCUSSION

DISCUSSION

The present study consisted a total of 63 patients, 25 diabetic and 38 non-diabetic dyspeptics, who were subjected to upper gastrointestinal endoscopy and rapid urease test . Out of the 25 diabetic dyspeptics, 18 (72%) patients were RUT+ve where as among the 38 non-diabetic dyspeptics, 20 (52.6%) patients were RUT+ve (table 1).Biopsy specimens from RUT-ve patients which were sent for histologic detection of *H. pylori* turned out to be positive in 2 diabetic dyspeptic patients and 1 control dyspeptic patient (table 2).

Thus this study showed a total prevalence of *Helicobacter pylori* in diabetic dyspeptic to be 80% where as in control dyspeptics to be 55.26%(table 3; $P<0.05$ but > 0.01).

This result appears quite similar to many other previous studies on comparable series (106-108,112,115,117,119-122) which have shown a significant correlation between *H. Pylori* and diabetes stating the possible role of autonomic neuropathy(95,122), microvascular complications and increased susceptibility of infection in diabetics (97,101,121).

In the present study prevalence of *H. Pylori* infection increased with increasing age in both diabetic & control dyspeptics with 70% in diabetic and 50% in control dyspeptics in 30-39 yrs. age group. The

prevalence reached 100% in diabetic and 80% in control dyspeptics in age group 50-59 years(table 4), which is in accordance with the usual trend of *H.Pylori* prevalence with age. The difference however was not statistically significant in our study .(P>0.1).

The prevalence of *H. Pylori* in male and female was similar (P>0.5). It was 76.9% and 54.5% in male diabetic and control dyspeptics respectively while 83.3% and 56.6% in female diabetic and control dyspeptics respectively(table 5) .

All our patient were from a low and middle socioeconomic status. None were from high socioeconomic group, which could be due to the reason that Bundelkhand is an economically backward area. In our study there was no significant difference in the prevalence of *H. pylori* in low and middle socioeconomic group(P>0.1). Prevalence in low socioeconomic group was 87.5% and 61.54% in diabetic & control dyspeptics respectively, while in middle socioeconomic group it was 66.7% & 41.67% in diabetic and control dyspeptics respectively (table 6).

Among diabetic dyspeptics, 85.7% *H. Pylori* +ve patients were hailing from rural areas, 85.7% were *H. Pylori* +ve patients and from the urban areas72.7% were *H. Pylori* +ve. Among control dyspeptic hailing from rural areas, 59.1% were *H. Pylori* +ve while from the

urban areas 50% were *H. Pylori* +ve ((table 7). The difference in the two groups was not statistically significant(P>0.1).

The complaints were similar in *H. pylori* +ve and *H. pylori* –ve groups in both diabetic & control dyspeptics. Belching with bloating was the most common complaint in diabetic dyspeptics (in 84% of diabetic dyspeptics) where as pain in abdomen/epigastric discomfort was the most common complaint in control dyspeptics (in 73.68% of control dyspeptics). Increased prevalence of belching and bloating in diabetics dyspeptics can be attributed to higher incidence of gastroparesis in diabetics.

In our study there was no significant correlation between duration of symptoms and prevalence of *H.pylori* (P> 0.5). The prevalence of H. Pylori in diabetics and control dyspeptics having complaints for < 1 year was 77.7% and 55.5% respectively, which was similar to the prevalence of *H. Pylori* in diabetics and control dyspeptics having complaints for > 1 year (81.25% and 55% respectively) (table 9). This shows that duration of complaints have no affect on *H. Pylori* prevalence.

With increase in duration of diabetes complications in diabetics also increase . Increase in incidence of microvascular complications and autonomic neuropathy may cause altered G.I. motility and promote *H. Pylori* colonization . In our study the prevalence of *H. Pylori* was significantly more in patients having diabetics for more than 5 years

(100%) as compared with patients with diabetes of duration less than 5 years (58.3%). (table 10;P<0.05)

In our study upper G.I endoscopy findings in *H. pylori* +ve diabetic dyspeptics showed gastritis in 65%,reflux esophagitis in 30%, duodenitis in30%, gastric ulcer in 10%,duodenal ulcer in 10% and normal finding in 35% patients.The results were quite similar to endoscopy findings in *H. pylori* +ve control dyspeptics which were gastritis in 52.4%,reflux esophagitis in 28.6%, duodenitis in 23.8%, gastric ulcer in 9.5%,duodenal ulcer in 9.5% and normal finding in 33.3% patients(table 11). No patient had en\vidence of malignancy on upper G.I endoscopy in either group.

Among H. pylori -ve diabetic dyspeptics maximum no. of patients had normal findings on upper G.I endoscopy followed by reflux esophagitis in 40% and gastritis in 20% patients. Among control dyspeptics upper G.I endoscopy findings showed normal finding in 70.5%, reflux esophagitis in 23.5%, gastritis in 11.7% and gastric ulcer in 5.6% patients.The findings in our study were similar to the usual trend in practice.

Autonomic neuropathy in diabetics by causing delayed gastric emptying (Gastroparesis diabeticorum) has been implicated in the increased prevalence of *H. Pylori* infection in diabetics. But in our study there was no significant difference in autonomic neuropathy between

both *H. Pylori* positive and *H. Pylori* negative diabetic dyspeptic groups. The prevalence of autonomic neuropathy was found to be 25% in *H. pylori* +ve patients and 20% in *H. Pylori* –ve patients . Thus other factors like increased susceptibility to infections and micorvascular complications in diabetics may be responsible for the increased *H. Pylori* prevalence in them.

SUMMARY & CONCLUSION

SUMMARY AND CONCLUSION

The present study "*Prevalence of Helicobacter pylori in diabetic and non diabetic dyspeptics patients in Bundelkhand region*" was conducted in the department of medicine, M.L.B. Medical College Jhansi .

A total of 63 patients were included in our study. Among which 25 were diabetic dyspeptics and 38 were age and gender matched non diabetic dyspeptic patients. These patients underwent detailed clinical evaluation, upper G.I endoscopy, rapid urease test and histopathalogical examination of the biopsy specimen . The data that emerged from the analysis can be summarized as follows.

1. Of the 25 diabetics dyspeptics, 80% were *H. Pylori* positive and among the 38 control dyspeptics 55.26% were *H. Pylori* positive. In our study prevalence of *H. Pylori* was significantly more in diabetic dyspeptics as compared with control dyspeptics ($P<0.05$).

2. H. pylori prevalence increased with age. *H. Pylori* prevalence was 70% among diabetic dyspeptics and 50% among control dyspeptics patients in 30-39 year age group whereas in age group 50-59 years it was 100% among diabetics dyspeptics and 80% among control dyspeptics patients. But the results were not statistically significant.

3. Among males and females *H. Pylori* prevalence was found to be similar in both diabetic and control dyspeptic groups.

4. No significant difference was found in the prevalence of *H. Pylori* in low and middle socio economic groups.

5. Similarily there was no significant difference in the prevalence of *H. Pylori* in rural and urban areas.

6. The most common complaint in diabetic dyspeptics was belching with bloating, whereas in control dyspeptics it was pain in abdomen / epigastric discomfort . In both the groups there was no significant difference regarding the presenting complaints between *H. Pylori* +ve and *H. Pylori* –ve patients.

7. In our study no significant difference was found between *H. Pylori* prevalence and duration of complaints in the two groups.

8. The prevalence of *H. Pylori* in patients having diabetes for less than 5 year was 58.3% where as in those having diabetes for more than 5 years was 100% . The difference was significant ($P<0.05$).

9. The upper G.I endoscopic findings were more in *H. Pylori* +ve diabetic and control dyspeptics while most of the *H. Pylori* negative control and diabetic dyspeptics had normal upper G.I endoscopy

findings. The pattern of endoscopic findings was similar in both diabetic and control dyspeptics patients.

10. The prevalence of autonomic neuropathy in *H. Pylori* +ve . and *H. Pylori* –ve diabetic dyspeptics was similar.

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Non Diabetic dyspeptic patients

S.No.	Name	Age /sex	Socioeco status	Rural/ Urban	TDI	Endo. findings	RUT	Histopath.	H.pylori status
1.	Shauqat	30/F	Low	rural	4 mon	Normal	+ve	NA	+ve
2.	Seema	35/F	Middle	urban	2 yrs	Normal	+ve	NA	+ve
3.	Balmukund	45/M	Low	rural	9 mon	Gastritis.+ duod.	+ve	NA	+ve
4.	Kholbara Das	40/M	Low	rural	3 yrs	GU+ reflux esoph	+ve	NA	+ve
5.	Luxmi	35/F	Middle	urban	10 mon	Gastritis	+ve	NA	+ve
6.	Khuman	30/M	Low	rural	4 mon	Normal	+ve	NA	+ve
7.	Chandra Pal	35/F	Low	rural	5 mon	Normal	+ve	NA	+ve
8.	Jagjeevan Ram	32/M	Low	urban	7 mon	Gastritis + reflux esoph	+ve	NA	+ve
9.	Vijay	32/M	Middle	urban	2 yrs	Normal	+ve	NA	+ve
10.	Amrat Lal	50/M	Low	rural	2.5 yrs	Gastritis.+ duod.	+ve	NA	+ve
11.	Achchay Lal	55/M	Low	rural	3 yrs	Gastritis.+ duod.	+ve	NA	+ve
12.	Shiv Lal	35/M	Low	rural	2 yrs	Gastritis.+ duod	+ve	NA	+ve
13.	Hem Lata	32/F	Middle	urban	8 mon	Normal	+ve	NA	+ve
14.	Sharanjeet Kaur	32/F	Middle	urban	4 mon	Normal	+ve	NA	+ve
15.	Prem Bai	55/F	Low	rural	3 yrs	Gastritis.+ duod.	+ve	NA	+ve
16.	Toran Singh	55/M	Low	rural	4 yrs	GU+ reflux esoph	+ve	NA	+ve
17.	Chandan Singh	32/M	Low	urban	5 mon	Gastritis+ reflux esoph	+ve	NA	+ve
18.	Hari Ram	40/M	Low	rural	1.5 yrs	DU+ Gastritis+ reflux esoph	+ve	NA	+ve
19.	Babu Singh	42/M	Low	rural	9 mon	Gastritis.+ duod	+ve	NA	+ve
20.	Shanti	47/F	Low	urban	2 yrs	DU+ reflux esoph	+ve	NA	+ve

Non Diabetic dyspeptic patients

S.No.	Name	Age /sex	Socioeco status	Rural/ Urban	TDI	Endo. findings	RUT	Histopath.	H.pylori status
21.	D. C. Puneet	30/M	Middle	urban	2.5 yrs	Normal	-ve	Colonies -nt	-ve
22.	Kishan Lal	48/M	Low	rural	5 mon	Gastritis + reflux esoph	-ve	Colonies -nt	-ve
23.	Satya Prakash	34/M	Middle	urban	3 yrs	Normal	-ve	Colonies -nt	-ve
24.	Chitra Sen	35/M	Low	rural	9 mon	Normal	-ve	Colonies -nt	-ve
25.	Chandra	32/F	Low	urban	2yrs	Normal	-ve	Colonies -nt	-ve
26.	Ram Pati	48/F	Low	rural	2yrs	Reflux esoph	-ve	Colonies -nt	-ve
27.	Munni Devi	35/F	Low	rural	4 mon	Normal	-ve	Colonies -nt	-ve
28.	Maya Devi	35/F	Middle	urban	4 mon	Normal	-ve	Colonies -nt	-ve
29.	Pista	48/F	Low	rural	5 mon	Normal	-ve	Colonies -nt	-ve
30.	Mehar Baan	58/M	Low	rural	3 yrs	GU+reflux esoph	-ve	Colonies -nt	-ve
31.	Pooran	30/M	Low	rural	2 yrs	Normal	-ve	Colonies -nt	-ve
32.	Raj kumari	35/F	Middle	urban	4 yrs	Gastritis + reflux esoph	-ve	Colonies -nt	-ve
33.	Jugal Kishore	38/M	Middle	urban	3 yrs	Normal	-ve	Colonies -nt	-ve
34.	Anand Pratap Singh	32/M	Low	rural	8 mon	Normal	-ve	Colonies -nt	-ve
35.	Santosh Jain	30/M	Middle	urban	5 mon	Normal	-ve	Colonies -nt	-ve
36.	Mirza Ali Beg	36/M	Low	rural	10 mon	Normal	-ve	Colonies -nt	-ve
37.	Prakash Wati	35/F	Low	rural	2 yrs	Gastritis	-ve	Colonies +nt	+ve
38.	Prakash	42/F	Middle	urban	1.5 yrs	Normal	-ve	Colonies -nt	-ve

Diabetic dyspeptic patients

S.No.	Name	Age /sex	Socioeco status	Rural/ Urban	TDI	Diab duration	Auto. neuropathy	Endo. findings	RUT	Histopath	H.pylo status
1.	Ram Vati	55/F	Low	rural	4 yrs	11 yrs	present	Gastritis.+ duod.	+ve	NA	+ve
2.	Kausaliya	48/F	Low	rural	2 yrs	12 yrs	present	Gastritis.+ duod.	+ve	NA	+ve
3.	Narendra Awasthi	38/M	Middle	urban	9 mon	4 yrs	absent	Gastritis + GU+ reflux esoph	+ve	NA	+ve
4.	Ram Das	40/M	Low	rural	2 yrs	6 yrs	absent	Gastritis.+ duod.	+ve	NA	+ve
5.	Anjani	35/F	Middle	urban	5 mon	4 yrs	absent	Normal	+ve	NA	+ve
6.	Vidhya Devi	35/F	Low	rural	10 mon	4 yrs	absent	Gastritis + DU+ reflux esoph	+ve	NA	+ve
7.	Urmilla	32/F	Low	urban	5 mon	4 yrs	absent	Gastritis + reflux esoph.	+ve	NA	+ve
8.	Asha Rawat	38/F	Middle	urban	10 mon	5 yrs	absent	Normal	+ve	NA	+ve
9.	B. D. Verma	42/M	Middle	urban	3 yrs	7 yrs	present	Gastritis + DU+ reflux esoph	+ve	NA	+ve
10.	Thakur Das	35/M	Low	rural	9 mon	4 yrs	absent	Normal	+ve	NA	+ve
11.	Ranjeet Singh	45/F	Middle	urban	1.5 yrs	6 yrs	absent	Gastritis.+ duod.	+ve	NA	+ve
12.	Sunil Kumar	40/M	Low	rural	2 yrs	5 yrs	absent	Normal	+ve	NA	+ve
13.	Shyam Narayan	43/M	Low	urban	3 yrs	11 yrs	present	Gastritis.+ duod.	+ve	NA	+ve
14.	Lala Ram	52/M	Low	rural	8 mon	6 mon	absent	Normal	+ve	NA	+ve
15.	Mohan Lal	40/M	Low	rural	2.5 yrs	5 yrs	absent	Gastritis.+ duod.	+ve	NA	+ve
16.	Veer Pratap Singh	40/M	Middle	urban	2 yrs	5 yrs	absent	Gastritis + reflux esoph	+ve	NA	+ve
17.	Pool Wati	48/F	Low	rural	1 yr	7 yrs	absent	Gastritis + GU+ reflux esoph	+ve	NA	+ve
18.	Bal Kumari	38/F	Low	rural	2 yrs	4 yrs	absent	Normal	+ve	NA	+ve

Diabetic dyspeptic patients

S.No.	Name	Age /sex	Socioeco status	Rural/ Urban	TDI	Diab duration	Auto. neuropathy	Endo. findings	RUT	Histopath.	H.pylori status
19.	Om Prakash	34/M	Low	rural	9 mon	2 yrs	absent	Gastritis + reflux esoph	-ve	Colonies -nt	-ve
20.	Laxman Prasad	42/M	Middle	urban	2 yrs	3 yrs	present	reflux esoph	-ve	Colonies -nt	-ve
21.	Khumano Bai	40/F	Low	rural	3 yrs	2 yrs	absent	Normal	-ve	Colonies -nt	-ve
22.	Pawan Kumar	34/M	Middle	urban	5 mon	4 yrs	absent	Normal	-ve	Colonies -nt	-ve
23.	B.S. Yogi	35/F	Middle	urban	2 yrs	3 yrs	absent	Normal	-ve	Colonies -nt	-ve
24.	Prema Devi	55/F	Low	rural	4 yrs	8 yrs	present	Gastritis. +duod	-ve	Colonies +nt	+ve
25.	Badri Prasad Gupta	52/M	Low	rural	1.5 yrs	9 yrs	absent	Normal	-ve	Colonies +nt	+ve